Contractures and Hypertonia of the Arm After Stroke

Development, Assessment and Treatment

Lex D. de Jong

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Chapter 1

Introduction

Background

Stroke, also known as a cerebrovascular accident (CVA), occurs when the arteries leading to certain areas of the brain rupture (hemorrhagic stroke) or get blocked (ischemic stroke). Without sufficient oxygen supply, brain cells die. Depending on the amount of brain tissue damage, the stroke results in weakness or paralysis on one side of the body. In neuroscientific terms, a stroke patient has sustained a lesion of the descending corticospinal system, a condition collectively termed the upper *motor neurone (UMN) syndrome*.

Stroke is a major public health concern. In Europe, more than 1.1 million stroke events happened in the year 2000 and the estimates are that it will happen to 1.5 million people each year by 2025.[1] In the Netherlands, about 41.000 people are struck by a stroke annually.[2] Half of all the surviving patients make incomplete recovery, and half of them need assistance in activities of daily life (ADL).[3] About 77-81% of stroke survivors show a motor deficit of the extremities.[4] In almost 66% of patients with an initial paralysis, the affected arm remains inactive and immobilised due to a lack of return of motor function after six months.[5,6] Damage to the UMN system is further characterised by both *negative* and *positive* motor signs, which can result in several individual health related problems. These problems contribute to stroke being the second most costly disease amongst the elderly, costs which are expected to increase by 40% by 2015.[7]

Negative and positive motor signs of the UMN syndrome

Negative motor signs ("signs of absence") after a stroke result from deficient voluntary muscle activity. In the hemiplegic arm these signs include muscle weakness, loss of dexterity and selective control of movement. For the patient this means that he/she is no longer able to selectively activate and control limb segments (in part or as a whole). This results in a limited ability to produce voluntary goal-directed motor actions. Because of the lack of motor recovery, the involved arm often becomes inactive and immobilised. The central nervous system and the muscular, vascular and connective tissues systems adapt to this state of immobilisation and inactivity.[8,9] Positive motor signs ("signs of presence") result from a variety of muscle overactivity types such as clonus, co-contractions and velocity-dependent increases in excitability of phasic and tonic muscle stretch reflexes. The latter is also known as spasticity. This neurologically induced phenomenon results from loss of inhibitory supraspinal control over spinal reflex activity.[10] Spasticity can affect the trunk, legs and arms. In fact, any of the positive motor signs can more or less impede voluntary motor actions, but spasticity in particular is associated with impairments in body functions and activity limitations.[11,12]

Two significant consequences of spasticity are that the spastic muscle has the tendency to remain in a shortened position for prolonged periods of time, and that attempted movements are restricted. Prolonged periods of both spasticity and immobilization result in the development of biomechanical changes of the muscles. These biomechanical changes can predispose a stroke patient to the development of muscle contractures.[13] Muscle contractures are characterized by a loss of functional motor units and changes in muscle fibre type. Muscles subject to prolonged positioning at a short length, and which are rarely exposed to active or passive stretch, also lose sarcomeres as a result of decreased protein synthesis. As a consequence, these muscles show an increase in the amount of connective tissue and become stiffer.[14] These secondary adaptations are particularly evident in antigravity postural muscles and appear quickly, have potent negative effects on the patient's ability to exercise, train and regain effective performance of motor actions.[15] The long held belief that contracture is a secondary complication of spasticity was recently supported by scientific evidence.[13] Despite this finding, there is still little evidence that decreasing spasticity has a positive effect on shoulder or arm muscle contractures.[(eg 16-18)] Conversely, the fact that hyperactivity could only be elicited toward the end of range in a muscle with contracture suggests that the presence of contracture may be a potentiator of the stretch reflex.[19] It is also possible that spasticity and muscle contracture are mutually potentiating.[20]

Hypertonia

An examiner will feel spasticity as a velocity-dependent increase in resistance to passive muscle stretch. The muscles most at risk of developing spasticity are also those that traditionally develop contractures. Contractures result in stiffer muscles, which also introduces an increase in resistance to stretch. Interestingly, many patients develop both spasticity and contractures in the shoulder extensors, adductors and internal rotators.[21] In these (and other) muscles, the combination of neurological and biomechanical resistance to passive stretch results in an impairment that is called *hypertonia.*

Post-stroke hypertonia has been associated with dependence in every-day activities,[22] motor impairments, activity limitations,[12,23] worse arm motor recovery and a longer time to admission for rehabilitation.[24] These findings suggest that hypertonia is an important and well monitored impairment after stroke. However, data about the incidence of hypertonia is scarce. Data about the prevalence of hypertonia is rather heterogeneous due to differences in patient groups (acute vs. chronic/ischemic vs. hemorrhagic stroke), assessment timing (ranging between 5.4 days and 18 months), methods of assessment (Ashworth Scale[25], Modified Ashworth Scale[26], Tone Assessment Scale[27]), study design (cross-sectional versus

longitudinal) and a multitude of clinical definitions used to define hypertonia.[22-24,28,29] Although some literature reports on how arm hypertonia evolves post-stroke,[28,30] to date little is known about whether hypertonia develops differently in specific subgroups of patients and whether it's development can be predicted. Another problem is that, clinically, the neurological (i.e. spasticity) and biomechanical (i.e. contracture) contributions to hypertonia cannot easily be distinguished. This does not allow clinicians and therapists to offer their patients tailored treatment, since this requires discrimination between the neural and tissue related components of hypertonia. Further research in this area would not be amiss.

Hemiplegic shoulder pain

Generally, hemiplegic shoulder pain (HSP) or post-stroke shoulder pain is prevalent in approximately 22-23% of the general population of stroke survivors,[31] and in almost 54% of patients in rehabilitation settings.[31,32] Much uncertainty exists as to the specific causes for the development of HSP. Since HSP is associated with reduced quality of life[33] and restricts patients' daily lives,[34] there is an urgent need to investigate the causes of HSP and interventions aimed at the prevention of HSP. Despite some contradicting findings, growing evidence exists indicating that spasticity might be the main cause of HSP.[35] Furthermore, loss of range of motion due to contracture is also associated with the occurrence of HSP.[36-40] The latter findings together suggest that there are bidirectional relationships between spasticity, contracture and HSP. This raises the question whether influencing either spasticity or contracture could result in a change in HSP.

Evidence based interventions for post-stroke spasticity, contracture and shoulder pain

Several interventions improve arm function after stroke and prevent secondary impairments.[eg.41-43] However, many of these interventions are not suitable for patients with severe motor deficits because these require 'active' residual arm motor capacity. Although literature does not provide a clear definition of "severe motor deficit", post-stroke recovery trends indicate that those who have the poorest level of recovery score around 18 points on the arm section of the Fugl-Meyer Assessment (FMA)[44] in the chronic phase post-stroke.[45,46] Especially in these patients the chances of arm recovery are diminished, and the development of hypertonia ('spasticity')[22,30] and contractures[8,47] are increased. These patients often lack the minimal motor abilities required to engage in interventions such as computerized arm training[48] or constraint-induced movement therapy.[49,50] Therefore, 'passive' interventions are needed to prevent secondary impairments and optimise long-term handling and assistive use of the affected arm.

In this thesis, the underlying bidirectional relationships between spasticity, contracture and HSP served as a theoretical framework to try and prevent the development of contracture after stroke with the aim of simultaneously preventing the development of hypertonia, spasticity and shoulder pain. Literature describes several of such 'passive' interventions. For example, a seemingly appropriate 'passive' intervention for patients with muscle overactivity (or abnormal muscular contractions such as spasticity) is the use of botulinum toxin.[51,52] However, botulinum toxin is only prescribed after spasticity has emerged[53] or poses a direct health-related problem for a patient. To date, there is no solid evidence that it can be used to directly influence the neural component of hypertonia in the earliest stages after stroke. Improvements in spasticity have also been seen in the use of repetitive transcranial magnetic stimulation (rTMS).[54,55] As promising as this recent intervention may seem, more work is needed to investigate the merits of this approach. Two other 'passive' interventions which appear to be appropriate are static arm muscle stretching programmes and neuromuscular electrical stimulation (NMES).

Static muscle stretching and neuromuscular electrical stimulation

The proactive application of specific arm muscle stretching programmes after stroke (i.e. to stretch the arm muscles prone to shortening for longer periods of time per day) was first recommended by Ada and Canning.[56] They derived their idea for this intervention in part from animal research, which showed that sustained passive muscle stretch resulted in an increase in sarcomere number.[57] Although the study of mechanisms of muscle contracture in humans is rather difficult, it has been assumed that muscles of humans undergo similar adaptations.[58] The results of the first study regarding the efficacy of such a static arm muscle stretching programme in patients after stroke were inconclusive,[59] thus meriting further research.

Investigations of the application of cyclic NMES[60] after stroke showed that it can be used to reduce glenohumeral subluxation[61,62] and reduce muscle resistance[63] resulting from reciprocal inhibition.[64-66] NMES can also be used as an electrically induced stretching exercise. This 'passive' exercise can improve pain-free range of passive humeral lateral rotation,[61] although reviewers have concluded that this is the only significant benefit.[67] Unfortunately it is unknown whether these results apply to patients with poor recovery of arm function, and whether it is easier to stretch (hypertonic) muscles in conjunction with NMES. In view of the reported benefits of NMES it may be worthwhile to investigate the effects of a static arm muscle stretching programme combined with NMES.

Reliability of passive range of arm motion measurements

To assess and evaluate the arm function of patients after stroke, clinicians and researchers can use a wide variety of assessment tools. Of these, goniometry gives insight into the active (AROM) and passive (PROM) range of joint motion. Unfortunately, little specific information about goniometric measurements in patients after stroke can be found in literature.

In patients with severe arm motor deficits after stroke, the degree of passive shoulder external rotation, abduction and wrist extension are regularly used as outcome measures to evaluate the effects of interventions.[eg. 67-69] First of all, valuable conclusions about changes in PROM can only be drawn when these measurements are reliable. Reliability of arm ROM measurements was shown to be good in healthy subjects[70,71] and in patients with orthopedic conditions.[72,73] These findings cannot simply be generalised to patients who have suffered a stroke since a large portion develop contractures, hypertonia, spasticity and shoulder pain. These impairments in body functions can hinder the rater's attempts to move the hemiplegic arm, and may increase the chance of making measurement errors. Performance of PROM measurements by one rater only may also increase these errors because simultaneously handling a paralyzed arm, the goniometer and reading the score is difficult. Identifying and quantifying these sources of variation is important in order to find strategies to reduce their influence on outcomes.[74]

Goniometric measurements of arm joints in patients after stroke reflect both the true range of a joint and measurement errors caused by different sources of variation. In general, a useful indicator to express real, non-error change in an outcome measure is the smallest detectable difference (SDD). In the case of goniometry for example, the SDD offers clinicians and scientists information as to whether a difference in PROM (over time) is due to random measurement error, or actually represents a true difference or change in their patients' PROM. Ideally, a difference in PROM from the start to the end of a treatment period should at least exceed the SDD to be able to conclude with 95% certainty that the PROM has really changed over time. Similarly, in addition to a statistical significant difference, a difference in PROM between an experimental and a control condition should exceed the SDD for the intervention to be called superior to the control condition. This knowledge can also serve to evaluate the benefit of a treatment based on individual patient improvement relative to both cost and risk of complications.[75] To date there is a dearth of literature regarding the reliability of PROM measurements in patients after stroke. Not only information regarding smallest detectable differences is lacking, but also regarding factors that might potentially influence hemiplegic arm PROM measurements. As a consequence, each time PROM results are presented, the question remains as to whether such measurements were reliable, reflect the

true change in PROM (instead of measurement error) and were influenced by different stroke-specific sources of variation. Therefore, these topics need to be investigated.

Outline of the thesis

In this thesis, the results of a cohort study and two multicenter randomized controlled trials (RCT's) that were designed and performed between 2002 and 2011 are presented. The aim of the cohort study, as described in *Chapter 2*, was to analyse the development of hypertonia in the hemiparetic elbow flexors, and to explore the predictive value of arm motor control on hypertonia in 50 first-ever stroke survivors in their first six months post-stroke. Because secondary complications such as hypertonia can have detrimental effects on hemiplegic arm use, shoulder pain and quality of life, several authors suggested that specific preventive static arm muscle stretching programmes should be incorporated into the rehabilitation therapy programme. The main aim of the RCT's that are presented in this thesis was to explore whether the clinical application of two such static arm muscle stretching programmes during rehabilitation could prevent the development of secondary impairments in patients after stroke with very poor arm motor control. In the first pilot RCT, the efficacy of a single-modality static arm muscle stretching programme was investigated. The results of this RCT will be presented in *Chapter 3*. The findings of this pilot trial, combined with findings from literature, gave clear reasons to investigate a similar static arm muscle stretching programme using a higher intensity of stretch. To achieve this, neuromuscular electrical stimulation was used as an adjunct to stretching. The results of this multimodal RCT are described in *Chapter 4*. During both RCT's, the passive joint ranges were assessed by two blinded observers. This not only presented the opportunity to report on interrater reliability, but also to generate information about smallest detectable differences and factors that were associated to, or influenced, the PROM measurements. The results of these studies will be described in *Chapter 5* and *Chapter 6.* Finally, *Chapter 7* contains the general discussion in which the results of the studies are integrated, the strengths and limitations of the studies are addressed and implications for future research and clinical practice are described.

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Chapter 2

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Arm motor control as predictor for hypertonia after stroke; a prospective cohort study

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Abstract

Objectives

To analyze the development of hypertonia in the hemiparetic elbow flexors, and to explore the predictive value of arm motor control on hypertonia in a cohort of first-ever stroke survivors in the first six months poststroke.

Design

A prospective cohort study.

Setting

A cohort of stroke survivors from a large, university-affiliated hospital in The Netherlands.

Participants

Patients (n = 50) with first-time ischemic strokes and initial arm paralysis who were admitted to a stroke unit.

Interventions

Not applicable

Main Outcome Measures

At 48 hours, 10 to 12 days, three and six months poststroke, hypertonia and arm motor control were assessed using the Modified Ashworth Scale and the Fugl-Meyer Assessment arm score.

Results

The incidence rate of hypertonia reached its maximum before the third month poststroke (30%). Prevalence was 42% at three and six months. Participants with poor arm motor control at 48 hours poststroke were 13 times more likely to develop hypertonia in the first six months poststroke than those with moderate to good arm motor control. These results were not confounded by the amount of arm function training received.

Conclusions

Hypertonia develops in a large proportion of patients with stroke, predominantly within the first three months poststroke. Poor arm motor control is a risk factor for the development of hypertonia.

Key Words

Epidemiology; muscle hypertonia; rehabilitation; risk factors; stroke; upper extremity.

Introduction

Annually, 15 million people worldwide have a stroke. Five million of them are left permanently disabled, placing a burden on both family and community.[1] In almost 66% of the stroke survivors with initial motor deficits, the affected arm remains without function after six months.[2,3] Because of this lack of function, the patient's affected arm remains inactive and immobilized. Over time, the central nervous system and (connective) tissues of the arm adapt to this state of inactivity,[4,5] often resulting in residual impairments such as contracture and hypertonia.

Poststroke hypertonia (increased resistance to passive stretch) has been associated with dependence in everyday activities,[6] motor impairments, activity limitations,[7,8] worse arm motor recovery, and a longer time to admission for rehabilitation.[9] Ideally, knowledge about epidemiologic data concerning hypertonia and its associated prognostic variables might help physiatrists and therapists to recognize how often it occurs and which patients are at greater risk of developing hypertonia so that preventive measures could be taken in daily clinical practice. However, data about the incidence of hypertonia are scarce, and until recently, only few postacute prognostic variables could be identified as a risk factor 12 months after stroke.[10,11] Besides that, the available data about the prevalence are rather heterogeneous because of differences in patient groups (acute vs chronic/ischemic vs hemorrhagic stroke), assessment timing (ranging between 5.4d and 18mo), assessment methods (Ashworth Scale, Modified Ashworth Scale, Tone Assessment Scale), study design (cross-sectional vs longitudinal), and the clinical definitions of hypertonia.[6,7,9,12,13] Moreover, because hypertonia may fluctuate over time in about 5% to 7.5% of the patients,[7,12,14] data from cross-sectional studies may underestimate or overestimate the prevalence of hypertonia.The two major contributors to hypertonia are reflex hyperexcitability and the passive mechanical properties of the muscle (contracture).[15] A more serious degree of upper motor neurone damage (ie, a larger stroke) results not only in less recovery[16] but also in the development of significantly more clinical manifestations such as reflex hyperexcitability.[17] In addition, full arm paralysis or severe paresis is likely to result in learned nonuse[18] of the hemiplegic arm, increasing the chance of contracture development. Since the combined effects of reflex hyperexcitability and contracture can cause increased resistance to passive stretch, one may expect that patients with stroke who have the most severe brain damage (and hence the poorest level of recovery of arm motor control) are more at risk for the development of hypertonia. Although some literature reports on how arm hypertonia evolves poststroke,[12,19] to date little is known about whether hypertonia develops differently in specific subgroups of patients. To test this hypothesis, subgroups have to be formed based on level of arm motor control. Findings from two recent studies showed

that patients with severe arm paresis had 10[19] to 22[6] times higher odds of having hypertonia at one month and one year poststroke, respectively, compared with patients with no and moderate paresis. However, in both studies, hypertonia was deemed present if resistance to passive movement was felt during any of eight different passive arm movements performed, which gives little detail about which muscles are most prone to hypertonia development. Moreover, one study[6] was a cross-sectional survey one year after stroke, presenting results from which it is difficult to predict who is (most) at risk of developing hypertonia and who may benefit from preventive intervention early after stroke onset. Collecting prospective data from single arm muscle groups would facilitate more accurate predictions. The aim of this study was twofold: (1) to analyze incidence and prevalence of hypertonia in the hemiplegic elbow flexors during the first six months poststroke and (2) to analyze the influence of motor control and time on the development of hypertonia. We hypothesized that (1) stroke survivors with poor recovery of motor control were more at risk for the development of hypertonia than those with a better level of recovery, and (2) the longer the period after stroke, the greater the risk for hypertonia.

Method

Participants and Study Design

The current study was part of a cohort study on the predictive value of transcranial magnetic stimulation (TMS) for recovery in ischemic stroke (M.H. Hoonhorst, unpublished data, 2011). The original cohort, 73 patients with first-ever ischemic strokes who were admitted to a specialized stroke unit of a large university-affiliated hospital (Isala Clinics, Zwolle, The Netherlands), was recruited between August 2005 and February 2008. Eligible participants were those who were unable to elevate the arm while lying in a supine position, unable to voluntarily move the fingers during the first physical screening, or both. After confirmation of the diagnosis by computed tomography or magnetic resonance imaging scan, the patient had to be hospitalized within the first day after the onset of symptoms and had to show a unilateral paralysis or significant paresis of the arm (Medical Research Council score, 0-3). Patients were excluded if they had severe loss of consciousness, were comatose, terminally ill, unable to receive neurorehabilitation because of severe comorbidity, or if contraindications for TMS were present.[20] In addition, patients without clear motor deficits within 24 hours of stroke onset (resulting from a transient ischemic attack) as clinically judged by the neurologist were also excluded. Each participant was assessed within 48 hours (t1), after 10 to 12 days (t2) and after three (t3) and six (t4) months postonset. All participants or close relatives gave written informed consent. The study was approved by the

local medical ethics committee.

Clinical Assessments

At baseline (t1), the participants' characteristics (age, sex, affected side) and Barthel Index scores were collected. Hypertonia was assessed using the six-point Modified Ashworth Scale (MAS),[21] which is a valid indicator of resistance to passive stretch.[15] During administration of the MAS, the participants were seated in a comfortable position with their forearms in supination. Participants were instructed to relax while the rater first passively moved the forearm from full flexion to full extension to determine the available range of motion. This was done slowly so as not to elicit any reflex activity. Then the same movement was repeated in approximately one second by counting "one thousand and one" to rate the actual resistance to passive movement. Clinically relevant hypertonia was operationally defined as an MAS score of at least 1+ (slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder [less than half] of the range of motion). Motor control of the hemiplegic arm was assessed using the 66-point arm section of the Fugl-Meyer Assessment (FMA).[22] The FMA has an excellent reliability, has good construct validity[23,24] and is highly responsive for changes in motor function after stroke.[25] We considered participants with an FMA score of 18 points or less as having poor motor control, and participants with more than 18 points as having moderate to good motor control. During the t2, t3, and t4 assessments, participants were additionally asked to report their weekly frequency of occupational therapy (OT) and physical therapy (PT), and whether arm function training (yes or no) was part of the treatment program in the weeks before the assessments. All assessments were performed in the hospital or outpatient location by the same rater (M.H.H.).

Statistical Analyses

Descriptive statistics were used to report participant characteristics at baseline. Incidence proportion (number of participants developing hypertonia during a time period/total number of participants at risk observed during that period) andprevalence (total number of participants showing hypertonia/total number of participants) were calculated for t1, t2, t3 and t4. At these time points, the frequency of OT and PT, and the number of participants receiving arm function training were compared between the two arm function groups (poor arm function vs moderate/good arm function) by using an independent *t*-test and a chi-square test, respectively. To estimate the predictive value of poor motor control and days after stroke for the development of hypertonia during the first six months, we dichotomised the MAS scores (MAS ≤1 and MAS ≥1+) and subsequently performed

a logistic generalized estimating equations (GEE) analysis by using an exchangeable correlation structure. With logistic GEE we predicted the dichotomous outcome variable (MAS) on the basis of a binary predictor variable (FMA ≤18 points at t1, *yes* or *no*) and an interval predictor variable (days after stroke), while correcting for dependency of the data within a participant (repeated assessments over time). The interaction between motor control and time was explored whereby time was recoded into days after stroke (t1-t4: 2, 11, 90 and 180 d, respectively). For all tests the two-tailed significance level was set at .05. All analyses were performed using SPSS (version 16).

Table 1 Characteristics of participants with a first-ever ischemic stroke at baseline (*n* = 50).

Characteristics	
Age (y)	70.3 ± 12.3
Sex (M/F)	21/29
Paretic side (L/R)	26/24
Barthel Index	5 (2-8.3)

Values are mean ± SD, n, or median (interquartile range).
Abbreviations: F, female; L, left; M, male; R, right.

Results

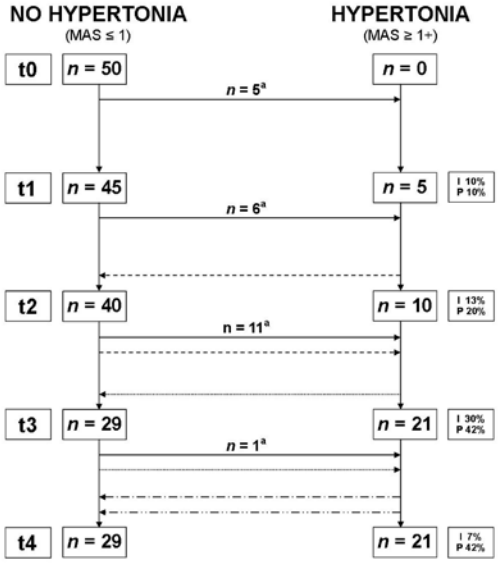
Of the initial 73 participants, 22 died and one was lost to follow-up (M.H. Hoonhorst, unpublished data, 2011), leaving 50 participants for data analysis. Their baseline characteristics are shown in Table 1. Figure 1 shows how hypertonia (the MAS scores) developed over time. Hypertonia incidence rate reached its maximum (30%) between t2 (10-12 d after stroke) and t3 (three mo after stroke); thereafter the incidence decreased. At six months poststroke (t4), 21 participants (42%) had hypertonia (MAS ≥1+), of whom four (8%) showed a transient course.

Table 2 Overall values of FMA armscores and percentages of participants with an FMA score of ≤18 points and >18 points at 48 hours (t1), after 10 to 12 days (t2), after three (t3) and six (t4) months.

FMA (n = 50)	t1	t2	t3	t4
Median (IQR)	8.5 (3–50.5)	17 (4–58)	51 (5.75–63)	53 (6–64)
≤18 points	60%	52%	38%	36%
>18 points	40%	48%	62%	64%

Abbreviations: IQR, interquartile range.

Figure 1 Flow chart depicting the development of hypertonia (MAS =1+), incidence proportions, and prevalence rates in/of 50 participants during the first six months poststroke. Solid arrows represent participants who developed permanent hypertonia. Dotted arrows represent the four individuals who showed a transient course of hypertonia.



Abbreviations: I, incidence proportion; P, prevalence rate; t0, prestroke; t1, at 48 hours; t2, at 10-12 days; t3, at three months; t4, at six months. [a]Number of participants who develop hypertonia for the first time.

Table 2 shows that 40% of the participants already had more than 18 points on the FMA at t1. This percentage increased to 64% at t4. At six months postonset, 36% of the participants had 18 points or less on the FMA, and their median FMA scores never exceeded a total of 5 points. In the other subgroup, recovery of arm motor control seemed to have stabilized at about three months poststroke with a median of 61 points. Between the two FMA-subgroups, no significant differences (*p*-values ranging from .074 and .98) with regard to the frequencies of OT and PT were found for any of the time points (Table 3). The total frequencies per group were also not significantly different (calculations not shown). Table 3 further shows that only 0% to 4% of the participants with more than 18 points on the FMA received arm training from physical therapists. Occupational therapists continued arm treatment in most participants irrespective of level of arm function until t3. After t3, only 13% of the participants with 18 points or less on the FMA continued receiving arm training from occupational therapists. Results from the GEE (Table 4) revealed that an FMA score of 18 points or less was a significant predictor for the

presence of hypertonia; these participants were 12.8 (95% confidence interval [CI], 3.5-47.3) times more likely develop hypertonia (MAS ≥1+). Days after stroke (time) also was a significant predictor of hypertonia; per day beta increased with .011. The interaction between motor control and time was not significant (p = .58).

Table 3 Between group comparison of possible confounders of arm hypertonia between 48 hours and six months poststroke.

	t1-t2		t2-t3		t3-t4	
	FMA ≤18	FMA >18	FMA ≤18	FMA >18	FMA ≤18	FMA >18
PT frequency (sessions/wk)	3.25 ± 0.53 (*n* = 24)	3.36 ± 0.58 (*n* = 22)	2.89 ± 1.05 (*n* = 19)	3.07 ± 1.08 (*n* = 30)	2.11 ± 0.96 (*n* = 18)	2.10 ± 1.35 (*n* = 31)
Participants receiving arm function training by physical therapist (%)	40%[a] (*n* = 20)	0%[a] (*n* = 16)	53%[a] (*n* = 15)	4%[a] (*n* = 24)	62%[a] (*n* = 13)	4%[a] (*n* = 24)
OT frequency (sessions/wk)	2.62 ± 0.65 (*n* = 24)	2.95 ± 0.58 (*n* = 22)	2.33 ± 1.09 (*n* = 18)	2.54 ± 1.14 (*n* = 26)	1.28 ± 1.07 (*n* = 18)	1.27 ± 1.46 (*n* = 30)
Participants receiving arm function training by occupational therapist(%)	100% (*n* = 21)	100% (*n* = 17)	87% (*n* = 15)	96% (*n* = 22)	13%[a] (*n* = 8)	73%[a] (*n* = 15)

Note: Values are mean ± SD or as otherwise indicated. *n* does not add up to 50 because of missing data. Abbreviations: PT, physical therapy; OT, occupational therapy; SD, standard deviation; FMA, Fugl-Meyer Assessment armscore.
[a] Significantly (X^2, Fisher exact test p<.05.) less OT from t3-t4 and more PT at all occasions for participants with poor motor control (FMA ≤18 points).

Table 4 Prediction of hypertonia (MAS ≥1+) in the first six months poststroke.

Predictors	Beta	SE	Sig.	OR (95% CI)
Poor arm motor control at t1	2.55	0.67	<.001	12.78 (3.46-47.25)
Days after stroke	0.011	0.004	.003	1.01[a] (1.00-1.02)
Constant	-3.17	0.56	<.001	0.04 (0.01-0.13)

Note. Results from generalized estimating equations (*n* = 50)
Abbreviation: SE, standard error; Sig., significance; OR, odds ratio; 95%CI, 95% confidence interval.
[a] It may seem that the effects of time can be neglected since the OR is 1.01 per day, but the influence of, for example, 30 days is considerable, resulting in an OR of $1.4 = e^{(30 * 0.011)}$.

Discussion

To our knowledge, this is the first longitudinal study describing in detail both the incidence and the prevalence of elbow flexor hypertonia in the first six months poststroke, as well as the predictive value of arm motor control on its development. The incidence rate of hypertonia reached its maximum before the third month poststroke (30%). A large portion (42%) of the participants had hypertonia at and six months postonset. The present study also shows that participants with poor motor control (ie, ≤18 points on the FMA) at 48 hours poststroke were 13 times more likely to develop hypertonia in the first six months poststroke than those with FMA scores of more than 18 points. Arm function training did not confound these findings. Additionally, the risk of developing hypertonia increased significantly over time.

Study Limitations

Some limitations of this study have to be addressed. First, only elbow flexor hypertonia was assessed using the commonly used MAS. Although there is considerable debate about the clinimetric properties of the MAS, several studies[26-28] have shown that its reliability is sufficiently high (eg, weighted kappa = .84 for interrater and .83 for intrarater comparisons[27]) when used to assess hypertonia in the elbow joint. However, because elbow flexors are not the only arm muscles prone to the development of hypertonia, the prevalence and incidence of hypertonia of the affected arm after stroke may have been underestimated in the current study. Second, because we dichotomized the MAS-scores, comparisons with the findings of other investigators may be hindered. We argue that clinically, MAS scores of 1 or less are not relevant, and patients with these scores do not receive interventions aimed at decreasing hypertonia. Further, in our opinion, the "catch and release" phenomenon as part of score 1 of the MAS is caused by a level of reflex hyperexcitability incapable of causing contracture. In addition, to be able to distinguish between no and clinically relevant hypertonia, the rater has to be able to detect clearly the differences in resistance to movement. When hypertonia was quantified biomechanically, subjects with an MAS of 1+ proved to have significantly higher resistance to passive movements than subjects with an MAS of 0 or 1,[29] which may be a prerequisite to detect these differences. However, in later research, differences in resistance between grades 1, 1+ and 2 could not be confirmed.[30] Future research is warranted to solve this issue. Third, only data of surviving participants were included in the analysis because they completed all assessments needed for the prediction model. Probably these participants had less extensive strokes than those who died in the course of the study. This selection probably resulted in an underestimation of incidence and prevalence data. Finally, the

amount of arm function training participants received from occupational and physical therapists during their participation did not confound the outcomes under study, but because some data were missing, the influence of arm function training needs further investigation in future studies.

In our study sample, the incidence rate of elbow flexor hypertonia was low at 48 hours and at 10 to 12 days (10%-13%), and reached a 30% maximum at three months post stroke with an additional 7% after six months. The prevalence steadily increased from 10% to 20% in the first 10 to 12 days to a maximum of 42% at three and six months poststroke. Comparison of these results with those of others (who claimed to have assessed spasticity, but who used the MAS and thus assessed hypertonia[30]) is hampered by differences in methodology. In a frequently cited prospective study by Sommerfeld et al.[7] (n = 95), an incidence rate of 21% was found at 5.4 days after stroke. Three months after stroke an incidence rate of 3% was found. The prevalence was 19% at that time. Their higher initial incidence rate could be explained by the cutoff point applied (MAS >0) and because the assessment was not limited to the elbow joint only. However, if this argument would be true, a higher incidence and prevalence would also be expected at three months poststroke in that study. More recently, a 4% incidence rate of hypertonia (MAS ≥1) at 2 to 10 days poststroke was reported. The prevalence was 23% at six months poststroke.[19] Since the cutoff point for hypertonia was lower than in our study, the differences between our studies cannot be explained adequately. Yet another definition of hypertonia (Ashworth Scale ≥2) was applied in a study[12] where hypertonia in the elbow and wrist was observed at time points similar to those of our study. The overall incidence rate in that study was very high: 63%. This high rate probably occurred because the most severely affected patients (suffering from first-ever or previous strokes) were selected in order to increase the chance of identifying risk factors for early or persistent hypertonia. Although no correlation was found between “early” hypertonia and previous stroke in that study, confounding (hypertonia from a previous stroke) may have affected the results. We therefore argue that it is best to only select patients with first-ever strokes.

The diversity in patient selection, joint assessment, moments of evaluation, and cutoff points for hypertonia illustrates the difficulty of comparing the different research results. Therefore a general overview of how many patients with stroke develop hypertonia can still not be given. What does seem clear, however, is that hypertonia develops predominantly within the first three months poststroke[12,14] and that it has a transient course in a small subgroup of patients.[7,12,14,19] We also observed these two patterns in our sample, resulting in a maximum incidence rate

and prevalence of 30% and 42%, respectively, and a transient course of hypertonia in 8% of our participants. This latter feature of hypertonia stresses the need for studying not only prevalences but also incidence rates by means of longitudinal study designs from the acute phase on.

To be able to analyze the influence of the level of motor control on the development of hypertonia, we divided our participants into two distinct FMA groups. We used an 18-point cutoff score because poststroke recovery trends indicate that those who have the poorest level of recovery score around 18 points in the chronic phase poststroke[31,32] and a score of less than 19 points within four weeks poststroke is a strong indicator for poor outcome at six months.[33] By applying this cutoff score we managed to make a clear distinction between those with poor arm motor control (typically showing only hyperreflexia and mass synergy patterns of shoulder internal rotation, finger and elbow flexion) and those with moderate to good motor control. In the current study, the poor recovery group represented 60% of the 50 participants at 48 hours and 36% at six months poststroke. During their participation, all participants received a comparable amount of OT and PT. Participants with the poorest level of arm motor control kept receiving arm PT onto six months poststroke. A comparable number of participants in both arm function groups received OT, which was discontinued in the poor function group only after arm motor control had stabilized at three months poststroke. This led us to conclude that arm training did not confound hypertonia development. However, one could instead argue that hypertonia was aggravated by the arm function training, a hypothesis that would require further investigation.

Results from our analysis showed that time was a significant contributor to hypertonia development. This was not surprising because both reflex hyperexcitability (resulting from reorganization within the central nervous system) and contracture (resulting from secondary soft tissue changes) need time to develop.[17] Although the resulting odds ratio (OR) suggests that the effect of time could be neglected (1.01 per day), the influence of, for example, 30 days is considerable, resulting in an OR of $1.4 = e^{(30 * 0.011)}$. Participants with poor arm motor control 48 hours poststroke had a 13 (95% CI, 3.5-47.3) times higher OR of developing hypertonia in the subsequent six months compared with those with moderate to good motor control. This result is in concordance with an OR of 10 (95%CI, 2.1-48.4) found in a nearly similar sample,[19] despite another definition of hypertonia (MAS ≥1 in any of four arm joints). In another study,[6] an OR of 22 (95%CI, 3.9-125) was found in a subgroup of participants with the most severe paresis. Despite our smaller sample size, our 95% CIs for the estimated ORs were smaller. Maybe our study sample was more

homogenous with respect to level of arm motor control. However, this assumption cannot be verified because of differences in arm motor control assessment. To analyze the effect of the cutoff point for the FMA, we performed a post hoc sensitivity analysis. The resulting ORs for poor motor control were 14.5 and 9.3 when using an FMA cutoff point of 9 and 36 points, respectively. These results indicate that the level of the cutoff point has an influence on the outcome, but they also show that the FMA is a fairly robust predictor of hypertonia development.

Our findings have shown that elbow flexor hypertonia develops in a considerable subgroup of patients with stroke. Our findings also imply that as early as 48 hours poststroke, one can predict who is most at risk for hypertonia development based on the FMA score. This knowledge might serve physiatrists and therapists to inform their patients about the risk of developing hypertonia. It might also serve therapists to take appropriate preventive actions (although a tailored treatment would require more detailed discrimination between the neural and tissue-related components of hypertonia). Despite these findings, hypertonia also developed in a number of participants with moderate to good arm function, which underscores the need for awareness of this impairment in all patients with stroke. As mentioned earlier, two of the main factors that contribute to hypertonia are reflex hyperexcitability and the passive mechanical properties of the muscle (contracture).[15] Reflex hyperexcitability may be hard to influence in the early stages after stroke. Physical and occupational therapists can, however, prevent contracture development in an attempt to keep down the level of resistance to passive movement. Patients with stroke who have an FMA score of 18 points or less could, for example, have measures implemented to prevent contractures. Such measures are currently not instituted soon enough after stroke.[34] Future prospective research should be performed to assess whether such measures, initiated in the acute phase poststroke, can help to reduce both the incidence and the prevalence of hypertonia and its associated features. To obtain a valid overall picture of the development of hypertonia, it seems paramount to perform more longitudinal research, to only select patients with first-ever strokes, to assess single joints separately, and to use similar definitions for hypertonia. In addition, it may be valuable to simultaneously assess clinical variables that seem to influence or predict the development of hypertonia, and to present raw data (Appendix 1) that enables better comparison between studies. Finally, we urge future researchers to abandon the use of the word ‘spasticity’ when, in fact, hypertonia (resistance to passive stretch) is assessed by using the MAS. This also implies reevaluation of epidemiologic data concerning spasticity as, for example, defined by Lance.[35]

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Appendix 1 Patient raw Fugl-Meyer Assessment (FMA) and Modified Ashworth Scale (MAS) data at 48 hours (t1), 10 to 12 days (t2), three (t3) and six months (t6) poststroke.

	t1		t2		t3		t4	
Participant	FMA	MAS	FMA	MAS	FMA	MAS	FMA	MAS
01	6	0	6	1	40	2	41	2
02	21	0	17	0	59	0	55	1
03	59	0	58	0	65	0	57	0
04	57	0	66	0	63	0	66	0
05	11	0	59	0	66	0	63	0
06	63	0	66	0	66	0	66	0
07	62	0	65	0	66	0	65	0
08	66	0	66	0	66	0	66	0
09	52	0	58	0	51	0	49	0
10	65	0	66	0	66	0	66	0
11	5	1	6	0	6	1	5	1
12	35	0	55	0	55	0	65	0
13	59	0	61	0	63	0	66	0
14	3	1	32	1	27	1	52	1
15	52	0	63	0	64	0	65	0
16	64	0	64	0	64	0	64	0
17	0	0	0	0	6	0	12	0
18	8	0	9	0	6	0	7	0
19	12	1+	17	1	34	3	38	3
20	5	0	3	0	2	0	1	1
21	3	0	4	0	6	2	8	2
22	5	0	58	0	62	2	64	2
23	2	0	20	1+	58	2	59	2
24	61	0	61	0	66	0	66	0
25	2	0	4	0	3	1+	3	2
26	63	0	65	0	65	1+	65	1
27	4	0	4	1+	10	2	9	2
28	4	1+	6	1+	4	2	6	3
29	9	0	7	1	4	0	4	0
30	2	0	6	1	6	1+	6	1+
31	12	0	12	0	60	0	62	0
32	5	1+	31	1+	36	2	27	2
33	5	1	32	1	61	1	61	1
34	38	1	53	1	65	0	65	0
35	7	0	7	1+	15	1	22	2
36	2	0	7	0	4	2	2	2
37	39	0	34	0	61	0	59	0
38	3	0	2	1	4	0	4	0
39	0	0	0	0	2	0	6	0
40	26	0	2	0	62	0	61	0
41	0	1	21	2	58	3	64	3
42	4	2	4	2	5	2	5	1
43	50	0	10	0	51	1+	54	2
44	46	0	1	1	4	1+	2	2
45	2	0	2	3	2	2	2	2
46	2	0	2	1+	2	2	2	2
47	3	2	15	3	24	1+	25	2
48	18	0	57	0	60	0	60	0
49	1	0	1	0	5	1	6	1+
50	42	0	56	0	59	0	59	0
	Median (IQR) 8.5 (3–50.5)	Median (IQR) 0 (0 – 0)	Median (IQR) 17 (4 – 58)	Median (IQR) 0 (0 – 1)	Median (IQR) 51 (5.75–63)	Median (IQR) 0 (0 – 3)	Median (IQR) 53 (6 – 64)	Median (IQR) 1 (0 – 3)

Note. The FMA arm score ranges from 0 to 66. Abbreviation: IQR, interquartile range.

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Chapter 3

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Contracture preventive positioning of the hemiplegic arm in subacute stroke patients: a pilot randomized controlled trial

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Abstract

Objective

To investigate the effectiveness of a contracture preventive positioning procedure for the hemiplegic arm in subacute stroke patients in addition to conventional physio- and occupational therapy.

Design

A single-blind pilot randomized controlled trial.

Setting

Inpatient neurological units from three rehabilitation centres in the Netherlands.

Subjects

Nineteen subacute stroke patients (minus two drop-outs) with a severe motor deficit of the arm.

Interventions

All subjects underwent conventional rehabilitation care. Nine subjects additionally received a positioning procedure for two 30-min sessions a day, five days a week, for five weeks.

Main measures

Passive range of motion of five arm movements using a hydrogoniometer and resistance to passive movement at the elbow using the Ashworth Scale.

Secondary outcome measures were pain at the end range of passive motions, the arm section of the Fugl-Meyer Assessment and Barthel Index scores for ADL-independence. Outcome measures were taken after five weeks and additional measurements after 10 weeks by two assessors blinded to group allocation.

Results

Comparison of the experimental (n = 9) with the control subjects (n = 8) after five weeks showed that additional positioning significantly slowed down development of shoulder abduction contracture (p = 0.042, -5.3 degrees versus -23 degrees). No other differences were found between the groups.

Conclusions

Applying a contracture preventive positioning procedure for the hemiplegic arm slowed down the development of shoulder abduction contracture. Positioning did not show significant additional value on other outcome measures. Since the sample size was small, results of this study need future verification.

Introduction

Hemiplegic shoulder pain is one of the most frequent complications after stroke.[1-5] Reviews of the literature[6-9] provide an overview of the different impairments of the shoulder joint and summarize the most effective therapeutic interventions to prevent hemiplegic shoulder pain. One of the factors associated with shoulder pain seems to be the loss of shoulder range of motion (ROM).[2,4,5,10] Poststroke contractures, as reflected by the loss of range of motion, are not surprising since increasing evidence supports the hypothesis that immobility after stroke is associated with changes in muscle due to adaptive mechanical and morphological changes in muscle fibres.[11,12] The proportion of patients with contracture in the hemiplegic arm approximately five months poststroke was reported to be as high as 54%.[13] In conjunction with contracture, resistance to passive movement[14] and spasticity develops in some patients.[13] Spasticity was found to be present in 26% of acute hemiparetic patients and in 28% three months after stroke in the study by Sommerfeld et al.[15] Spasticity (or more specifically, hypertonus) seems to be another cofactor in the development of hemiplegic shoulder pain.[6] It is related to a decrease in joint passive range of motion[16] and correlates both to motor impairments[15,17] and limitations in activities of daily living (ADL).[18]

Considering the above discussed impairments in and around the hemiplegic shoulder it is hypothesised that prevention of contracture[11,12,14,19] and maintaining an optimal pain free range of joint motion[6] is an important therapeutic intervention in stroke rehabilitation. Several authors suggest and describe different methods to prevent contracture (i.e. different positioning procedures).[11,20]

Recently, Ada et al.[21] showed for the first time that upper-limb positioning prevented shoulder external rotation contracture. However, questions remain as to whether recovery of selective arm movements, spasticity, pain and independence in activities of daily life (ADL) were affected by this intervention. Therefore, the present pilot trial addressed the following questions: Does a positioning procedure for the hemiplegic arm prevent (1) contracture as reflected by a decrease in passive range of motion and (2) increased resistance to passive movement. Second, does a positioning procedure have an effect on pain, motor performance of the arm and independence in ADL.

Methods

Study design

A single-blind randomized controlled, multi-centre trial was designed to investigate the effectiveness of a well-defined positioning procedure for the hemiplegic arm in subacute stroke patients. Rather than the positioning procedure(s) used in previous studies by Dean et al.[22] and Ada et al.[21] we additionally applied stretch to

the elbow flexors. The study was approved by the local medical ethics committee. All subjects gave written informed consent prior to participation.

Participants / Subjects

Using a sampling method of convenience, subjects were recruited from three rehabilitation centres in the Netherlands (Apeldoorn, Doorn and Zwolle). All stroke patients admitted between March 2003 (one centre participated as from January 2004) and January 2005 were initially screened by a physician.

Subjects had to meet the following inclusion criteria: (1) first ever stroke as defined by the World Health Organization[23] and maximally 12 weeks poststroke; (2) a medial cerebral artery stroke, established by means of computerized tomography/ magnetic resonance imaging (CT/MRI); (3) no premorbid impairments of the affected arm; (4) no severe shoulder pain; (5) no use of antispasticity drugs; (6) no use of pain-reducing drugs except for paracetamol, (7) no planned date of discharge and (8) able to give written informed consent. Subjects with fair to good recovery of the arm (as defined by Brunnstrom's stages of recovery 4, 5 or 6[24] and judged by the physician) were excluded. Patients who met the inclusion criteria were then referred to a physiotherapist, who administered tests to exclude patients with (9) severe neglect (a difference of more than three O's on the letter cancellation test,[25] severe loss of position sense (scores 2 and 3 on the Thumb Finding Test[26,27]) and cognitive impairment scoring lower than 23 points on the Mini-Mental State Examination.[28-30] Subjects with aphasia that could not answer the questions of the Mini-Mental State Examination were tested by means of the language comprehension subitems of the Akense Afasie Test[31] (minimum 67 points). Finally, patients who were able to prevent contracture by producing voluntary movement, having a Fugl-Meyer arm score of more than 18 points on the shoulder/elbow/ forearm subscales,[32] were excluded.

Primary outcome measures

Primary outcome measures were (1) passive range of motion using a masked fluid-filled goniometer (MIE Medical Research Ltd., Leeds, U.K.) and (2) resistance to passive movement using a Dutch translation of the original 5-point Ashworth Scale.[33]

Passive range-of-motion measurements

For standardization purposes of the passive range of motion testing procedures the assessors were trained beforehand,[34,35] shoulder abduction was applied during several shoulder movements[34,36,37] and two raters were used simultaneously. The first rater carried out one 'warming-up' movement prior to the actual passive

movement, the second rater measured the maximum range with a masked goniometer. Interrater reliability of the measurement protocol was explored simultaneously. Intraclass correlation coefficients (ICC type 3,1) were calculated for three different datasets, representing the three different evaluations with respectively 18, 13 and 12 subjects. ICC's were high, ranging between 0.78 and 0.99 (detailed procedures and results will be published elsewhere).

Ashworth grading of resistance to passive movement

Reliability of the original Ashworth Scale in stroke subjects was established for the elbow flexors.[38] We developed and used a Dutch translation of the original Ashworth Scale and simultaneously explored the interrater reliability of this translation. Agreement between our two raters when rating the resistance to passive extension of the elbow during the three different evaluations was fair to moderate (percentages of agreement between 67% and 83%, weighted kappa ranging from 0.484 to 0.773). The Ashworth gradings were administered according to the recommendations of Bohannon & Smith[39] and Koolstra et al.[40]

Secondary outcome measures

Secondary outcome measures were (3) pain, (4) motor performance of the hemiplegic arm and (5) independence in ADL. Subjects were asked to report if they felt pain at the end range of each passive motion (0 = no pain, 1 = pain). Motor performance was assessed using the 66-point arm section of the Fugl-Meyer Assessment,[32] a test that is both valid[41,42] and reliable[42-45] and assesses the subject's reflexes, the ability to perform 21 different volitional arm movements and co-ordination on an ordinal scale. Independence in ADL was assessed using a validated and reliable Dutch translation of the Barthel Index.[46]

Sample size

A pretrial power analysis was conducted using published data of shoulder external rotation range of motion of the involved shoulder joint in hemiplegic people.[2,4,10,37,47,48] When a power of 80% was used with a standard deviation of 20 degrees and a significance level of 0.05 (two-sided), 17 participants were required for each group.

Procedure

Subjects were randomly assigned to one of the two groups using opaque, sealed envelopes containing leaflets with either a capital A (experimental group) or a capital B (control group). Anticipating a patient drop-out of 10%, a total of 38 envelopes (19 As, 19 Bs) were distributed over three separate boxes to make

sure that both groups were evenly distributed over both arms of the study. An independent person carried out the randomization procedure. The envelopes were shuffled and drawn blindfolded. Treatment was initiated immediately after baseline measurement and within one week of the randomization procedure. Outcome measurements were taken five weeks later. Final measurements took place ten weeks after baseline measurements. The same two raters, unaware of group allocation and not involved in the treatment of subjects, carried out all the measurements. Blinding was achieved by reminding the subjects before every measurement that they should not reveal allocation to the observers.

Intervention: the positioning procedure

All subjects received 'conventional' rehabilitation treatment according to their clinical need as prescribed by the subject's primary care rehabilitation physician. Additionally, the subjects allocated to the experimental group were asked to carry out the prescribed positioning procedure for five weeks, twice a day for half an hour on weekdays (a total of 25 h in five weeks). Subjects still admitted after five weeks were asked to participate another five weeks for follow-up purposes. Positioning was carried out by the nursing staff under supervision of trained research physical therapists who instructed how the positioning procedure should be carried out. Care was taken that while moving the arm into position, the shoulder was moved with sufficient external rotation to avoid impingement or damage to the rotator cuff muscles. The arm was positioned with as much shoulder abduction, shoulder external rotation, elbow extension and supination of the forearm as the subject could endure without any pain. The arm was always supported by a pillow and, if necessary, held in position with a sandbag (Figure 1).

Patients were instructed not to change the position of the trunk to keep the m. pectoralis major elongated. Nursing staff registered whether the procedure was carried out as prescribed and noted possible deviations. Subjects allocated

Figure 1 The experimental positioning procedure.

to the control group received no additional therapy or positioning procedures.

'Contents of treatment sessions'
To document the contents of each physio- and occupational therapy session during the 10 weeks of the experiment, therapists were asked to complete a checklist after every therapy session. The checklist was based upon the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization.[49] By keeping this sort of therapy diary, possible confounding effects of the type and amount of (movement) therapy for the arm were recorded.

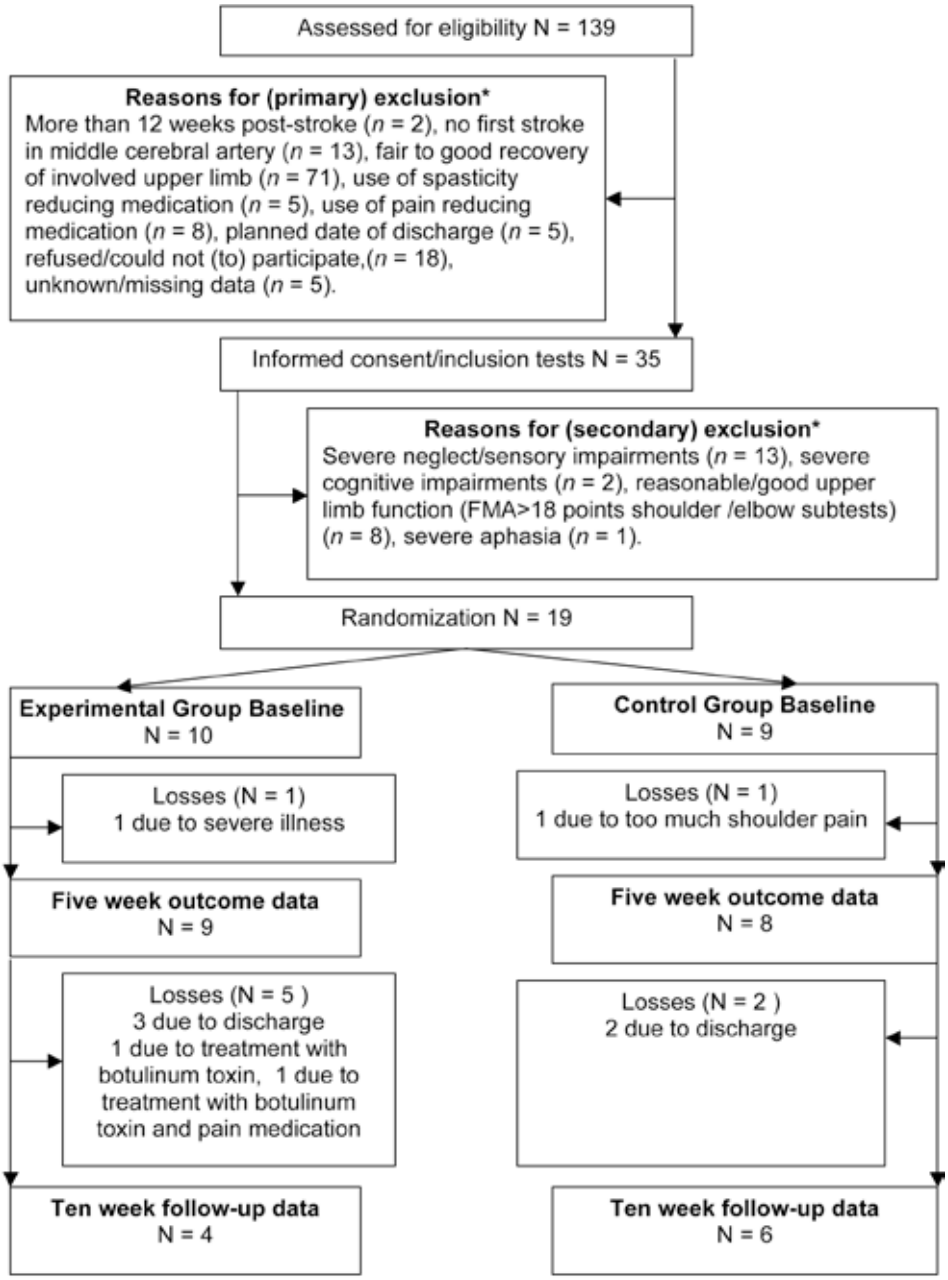
Statistical analysis

Ratio-level characteristics of subjects in the experimental and control group were compared using a Student's t-test and nominal level characteristics by means of a chi-square test. All primary and secondary outcome measures were compared at baseline and at five weeks between groups using the Student's t-test (range of motion), Mann-Whitney U-test (Ashworth Scale, Fugl-Meyer Assessment, Barthel Index) and a chi-square test (pain score). One subject from the experimental group (who fell too ill to participate any further) and one from the control group (who developed severe shoulder pain and refused further measurements) were not included in the analyses because of drop-out before the five week measurement (Figure 2). Results of the 10-week measurements between the groups were not analysed statistically due to the small sample size and high drop-out rate. All statistical procedures were carried out using SPSS for Windows (version 10.0.5). Level of significance was set at $p = 0.05$.

Results

Figure 2 shows the flow of subjects through each stage of the trial. Half of all eligible subjects were judged as already having reached Brunnstrom's fourth stage of recovery on admission, and were thus excluded. Eventually, only 19 subjects met all inclusion criteria and were randomly assigned to the experimental group (n = 10) or the control group (n = 9). The nine men and eight women who completed the study were between 36 and 63 years of age. Eleven out of 17 subjects had an affected left side (right hemisphere). Subjects from the experimental group started to use the positioning procedure around a mean (SD) of 35.7 (8.2) days poststroke. There were no differences between the groups with respect to these characteristics. As shown in Table 1, both groups received a comparable total amount of time spent on physio- and occupational therapy. The experimental group received more physiotherapy and less occupational therapy for the hemiplegic arm after five weeks, but the differences were not statistically significant.

Figure 2 Flow of subjects through each stage of the RCT from initial screening by rehabilitation physician to outcome measurement.



* If subjects were excluded for more than one reason, all reasons were mentioned separately.

Table 1 Means (standard deviations) of content of treatment sessions and time spent in the positioning procedure at five weeks.

Variable	At five weeks		
	EXP (n = 9)	CON (n = 8)	P-value
Total of OT (hours)	7 (1.8)	7.1 (3.4)[a]	0.915
Upper limb OT (hours)	2.1 (1.7)	3.2 (2.4)[a]	0.282
Total of PT (hours)	11.7 (3.2)	11.6 (2.6)	0.930
Upper limb PT (hours)	1.6 (1.4)	0.9 (0.6)	0.246
Total of positioning (hours)	19.9 (1.9)	0 (0)	<0.001

EXP, experimental group; CON, control group; OT, occupational therapy; PT, physiotherapy.
a Data from 1 control subject missing.

The nine subjects from the experimental group had the hemiplegic arm positioned for an average of approximately 20 hours (80% compliance to intervention).

Five week outcome measurements

Mean passive range of all motions were comparable in both groups at entry into the study (Table 2). It is of note that the shoulder external rotation and flexion ranges tended to be larger in the experimental group, but these differences were not significant. In the course of the first five weeks a clear decrease was seen in the range of motion of both groups, especially in the shoulder movements. After five weeks, shoulder abduction range of motion was significantly greater in the experimental group (p = 0.042). Table 2 also shows that none of the other movement directions were significantly different between the groups. Table 3 shows that the median Ashworth gradings were not different between the groups on entry into the study (p = 0.60). Despite a slight increase in both groups after five weeks, the differences between the groups did not reach significance (p= 0.917). Subjects from the experimental group started out with higher median scores on the Fugl-Meyer Assessment than the controls (16 versus 8.5 points), but this difference was not significant between the groups. After five weeks the subjects from the experimental group improved their ability to make selective movements of the hemiplegic arm. The control group on the other hand hardly showed any improvements at all. The difference between the groups was significant (p = 0.038). Both groups showed improvements in independence in ADL during the five weeks of participation. Barthel Index scores did not differ significantly at entry of the study or after five weeks. Of all participating subjects, approximately 65% reported pain at the end range of the shoulder movements and 35% of the elbow and forearm movements. There were no significant differences between the groups at this point. The pain at end of motion the subjects reported in the elbow and forearm hardly changed over the

Table 2 Between group comparisons of the mean passive range of motion (SD) and pre-post change scores after five weeks.

	At baseline			At five weeks			Change scores	
Variable	EXP (*n* = 9)	CON (*n* = 8)	P-value	EXP (*n* = 9)	CON (*n* = 8)	P-value	EXP (*n* = 9)	CON (*n* = 8)
ER	50.9 (24.9)	40.9 (24.5)	0.417	31.7 (24.5)	22.5 (14.7)	0.372	-19.2 (8.4)	-18.4 (15.6)
FLX	143.4 (21.8)	132.9 (26.8)	0.384	120.1 (31.7)	104.1 (27.5)	0.287	-23.3 (19.6)	-28.8 (27.5)
ABD	82.9 (11.6)	84.6 (13.1)	0.775	77.6 (12.9)	61.6 (16.7)	0.042	-5.3 (18)	-23 (13.1)
EXT	93.8 (11.7)	97.4 (8.8)	0.489	94.4 (10.7)	93.4 (11.2)	0.843	0.6 (3.3)	-4 (5.6)
SUP	77.1 (16.1)	72.1 (12.7)	0.493	65.6 (14.5)	69.4 (23.5)	0.688	-11.5 (9.5)	-2.7 (12.7)

ER, shoulder external rotation; FLX, shoulder flexion; ABD, shoulder abduction; EXT, elbow extension; SUP, forearm supination.

first five weeks, but increased for the shoulder movements to approximately 76% of the subjects. Again, there were no significant differences between the groups.

Ten week measurements

Having participated for five weeks in the primary study, 10 subjects were able to participate for a further period of five weeks. During these five weeks, the remaining four subjects from the experimental group received considerably more hours of physio- and occupational therapy and had the hemiplegic arm positioned for an additional average of 19 hours (76% of compliance to intervention). Added to the first five weeks, this made a total of 39 h of positioning (78% compliance to total intervention). Ten-week data are shown in Table 4.

Discussion

The aim of this pilot study was to investigate the effectiveness of a contracture preventive positioning procedure for subacute stroke patients with a severe motor deficit of their hemiplegic arm. Despite this therapeutic intervention, both groups showed a clear decrease in the passive range of motion of most arm movements. Applying the positioning procedure for five weeks slowed down the development of shoulder abduction contracture. Descriptive analysis of the 10-week measurements showed further decreases of passive range of motion in both groups. No significant differences were found between the groups with respect to resistance to passive stretch at five weeks. Fugl-Meyer Assessment scores in the experimental group

Table 3 Between-group comparisons of the medians (interquartile range) of the Ashworth Scale, Fugl-Meyer arm score and Barthel Index and pre-post change sores after five weeks.

	At baseline			At five weeks			Change scores	
Variable	EXP (*n* = 9)	CON (*n* = 8)	P-value	EXP (*n* = 9)	CON (*n* = 8)	P-value	EXP (*n* = 9)	CON (*n* = 8)
AS-EE	1 (1-2)	1.5 (1-2)	0.597	2 (1-2.5)	2 (1-2)	0.917	1 (0-1)	0 (0-0.75)
FMA	16 (8.5-21[a])	8.5 (7.25-22[a])	0.440	25 (15-38)	9 (8-26.5)	0.038	11 (3.5-20)	1 (0-5.75)
BI	13 (8.5-15.5)	14 (11.25-14.75)	0.530	18 (16-19.5)	17.5 (15.25-19.75)	0.770	6 (3-7)	4 (1.5-6.75)

AS-EE, Ashworth grade for elbow extension; FMA, Fugl-Meyer Assessment arm score; BI, Barthel Index. [a] Three subjects from the experimental group and two from the control group improved to >18 points on the FMA between inclusion test and baseline measurement.

Table 4 Means (standard deviations) of the different variables of the remaining 10 subjects after 10 weeks of positioning.

Variable	Experimental group (*n* = 4)	Control group (*n* = 6)
Total of OT (hours)	17.2 (6.8)	13.9 (7.6)[a]
Upper limb OT (hours)	6.2 (8)	3.2 (2.8)[a]
Total of PT (hours)	24.1 (6.7)	20 (3.6)
Upper limb PT (hours)	5.2 (3.6)	0.9 (0.7)
Total of positioning (hours)	38.8 (5.2)	0 (0)
PROM-ER	26.3 (23.7)	5.17 (5.64)
PROM-FLX	121 (27.8)	89.5 (22.7)
PROM-ABD	76 (16.8)	61.67 (8)
PROM-EXT	102.8 (16.1)	88.33 (6.4)
PROM-SUP	60.3 (17.7)	56.3 (16.4)
AS-EE (median ± IQR)	2 (1.25-2)	1.5 (1-3)
FMA (median ± IQR)	40.5 (30.75-45.75)	10 (8-17.25)
BI (median ± IQR)	20 (18.5-20)	18.5 (15.75-20)

PROM, passive range of motion; ER, shoulder external rotation; FLX, shoulder flexion; ABD, shoulder abduction; EXT, elbow extension; SUP, forearm supination; AS-EE, Ashworth grade for elbow extension; IQR, interquartile range; FMA, Fugl-Meyer Assessment arm score; BI, Barthel Index. [a] Data from 1 control subject missing.

were already larger on entry into the study, a difference that reached significance after five weeks. This trend seemed to continue after 10 weeks for the remaining subjects of the experimental group, but was probably biased by baseline differences. The percentage of subjects with pain at the end range of the shoulder movements remained high in both groups from baseline to 10 weeks. Especially in the first five

weeks of the trial the participating subjects of both groups gained more independence of ADL function as indicated by the Barthel Index.

One major limitation of this study was that it was underpowered. We aimed to select 34 sub-acute stroke patients, but after nearly two years the trial had to be terminated because of set time limits, leaving only 19 subjects who met all inclusion criteria. This suggests that the inclusion criteria were too strict. However, most patients were excluded because we considered their arm function as too 'active' for a 'passive' preventive positioning procedure. Therefore, the patients included in this study were representative of the target population, confirming the appropriateness of this inclusion criterion. Since only stroke patients eligible for clinical rehabilitation services were included in this study, persons with severe stroke and/or severe cognitive disabilities were excluded, hence reducing the external validity of the study.

Another possible limitation of the study was that the positioning procedure was carried out by several different nurses under the supervision of four physiotherapists trained in carrying out the positioning procedure. Regular checks of the positioning procedure by an independent assessor would have increased the rigor of this methodology. The current procedure however reflected the standard method of working in a Dutch rehabilitation center. Compliance to the protocol was not perfect (80%) because some subjects went on an early weekend leave.

Prevention of contracture in stroke patients is deemed very important in the stroke rehabilitation literature.[11,20] Dean et al.[22] reported unclear effects of a contracture preventive positioning protocol, mainly attributed to limited sample size and insufficient dosage. Ada et al.[21] found that 30 minutes of daily positioning for four weeks significantly prevented shoulder external rotation contracture. Compared to the procedures used by Dean et al. and Ada et al. we also stretched the elbow flexors using a positioning procedure that was prescribed for 60 minutes each working day for five consecutive weeks over and above standard physio-and occupational therapy.

As in the study of Dean et al., our subjects started the experimental positioning procedure in or around their fifth week poststroke, three weeks later than the subjects in the study by Ada et al. Dean et al. found a mean of respectively 11 and 14 degree decrease in the experimental and control group of shoulder external rotation after six weeks of positioning. Ada et al. found decreases of 6.1 and 17.9 degrees respectively after five weeks. In line with those results, our subjects showed not only a 19.2 (experimental group) and 18.4 (control group) decrease in shoulder

external rotation, but also decreases in shoulder abduction and flexion. Despite the apparent decreases of the range of motion, shoulder abduction was significantly larger in our experimental group after five weeks. Given the nearly similar positioning procedures to the study of Ada et al., no other explanation can be given for the lack of benefit in shoulder external rotation except for the difference in statistical power or the differences in fixation, allowing the weight of the lower arm to pull the shoulder joint into more or less external rotation. Resistance to passive movement of the elbow flexors as quantified by the Ashworth Scale was not influenced by the positioning despite the (submaximal) stretching of the elbow flexors.

In this study, motor performance was assessed by the arm section of the Fugl-Meyer Assessment. The score on this measure represents the capability of making several synergistic movements, and so it is not an objective measure of useful *functional* motor performance. Despite the fact that motor performance recovered significantly more in the experimental group, it is unlikely that the passive stretching procedure alone led to significant differences in motor performance. The experimental group's higher baseline scores possibly emphasized the motor scores after five weeks. The effect of more arm therapy between five and 10 weeks probably biased this difference even more. At the start of the study, nearly 65% of all subjects (n = 17) had pain at the end range of shoulder motions. This is in concordance with the findings of other authors.[1,4,5] Five weeks into the study, 76% of all subjects reported pain at end of motion and of the remaining 10 participants after ten weeks 83% still reported pain. Pain felt at the end range of motion was present and increased in both groups during the trial. It is unlikely that this was caused by the positioning procedure. As no single subject reported an inconvenience during the positioning procedure it seems justified to conclude that this kind of positioning is safe and harmless as long as it is performed within the patients' pain limits.

Fifteen to 30 minutes of daily stretching may be enough for healthy active animal muscles to prevent contracture[50,51] but positioning procedures for hemiparetic arms of stroke patients examined so far at the very most only seem to slow down the development of some contracture(s). To uncover larger significant effects, maybe the positioning procedure should be applied for more than one hour each day. However, we doubt that this is feasible within a clinical rehabilitation setting because of all the other time-consuming therapeutic activities during the day.

Slowing down the development of contractures using positioning procedures may be a prerequisite for the recovery of arm function, but we argue that combinations of more types of treatment are needed to have more impact on hemiplegic arm

recovery. Especially stroke patients with very poor arm function could benefit from combined preventive measures since they have limited abilities to 'actively' train their hemiplegic arm. Positioning procedures in conjunction with the use of electrical stimulation, for example, could be one such measure. Future randomized trials with larger sample sizes need to be performed to be able to support either a single- or multimodality treatment hypothesis.

Conclusion

We set out to investigate if a positioning procedure for the severely affected hemiplegic arm prevented contracture as reflected by a decrease in passive range of motion. We found some, but no solid evidence that a five-week positioning procedure slowed down the development of shoulder abduction contracture. Positioning had no clear influence on motor performance of the arm, resistance to passive movement of elbow flexors ('spasticity'), pain at the end range of five different arm motions and ADL-independence. In conclusion, preventive effect of a single-modality positioning procedure in addition to conventional physio- and occupational therapy still remains unclear for patients more than five weeks poststroke.

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Clinical messages

- Preventive positioning of the hemiplegic arm has a small beneficial effect on passive shoulder abduction passive range of motion in addition to conventional physio- and occupational therapy.
- Effects of positioning procedures on spasticity, motor performance, pain and independence in activities in daily life still remain unclear.

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Chapter 4

Lex D. de Jong | Pieter U. Dijkstra | Johan Gerritsen | Alexander C.H. Geurts | Klaas Postema

Combined arm stretch positioning and neuromuscular electrical stimulation during rehabilitation does not improve range of motion, shoulder pain or function in patients after stroke: a randomised trial

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Abstract

Question

Does static stretch positioning combined with simultaneous neuromuscular electrical stimulation (NMES) in the subacute phase after stroke have beneficial effects on basic arm body functions and activities?

Design

Multicentre randomised trial with concealed allocation, assessor blinding, and intention-to-treat analysis.

Participants

Forty-six people in the subacute phase after stroke with severe arm motor deficits (initial Fugl-Meyer Assessment arm score ≤ 18).

Intervention

In addition to conventional stroke rehabilitation, participants in the experimental group received arm stretch positioning combined with motor amplitude NMES for two 45-minute sessions a day, five days a week, for eight weeks. Control participants received sham arm positioning (ie, no stretch) and sham NMES (ie, transcutaneous electrical nerve stimulation with no motor effect) to the forearm only, at a similar frequency and duration.

Outcome measures

The primary outcome measures were passive range of arm motion and the presence of pain in the hemiplegic shoulder. Secondary outcome measures were severity of shoulder pain, restrictions in performance of activities of daily living, hypertonia, spasticity, motor control and shoulder subluxation. Outcomes were assessed at baseline, mid-treatment, at the end of the treatment period (8 weeks) and at follow-up (20 weeks).

Results

Multilevel regression analysis showed no significant group effects nor significant time × group interactions on any of the passive range of arm motions. The relative risk of shoulder pain in the experimental group was non-significant at 1.44 (95% CI 0.80 to 2.62).

Conclusion

In people with poor arm motor control in the subacute phase after stroke, static stretch positioning combined with simultaneous NMES has no statistically significant effects on range of motion, shoulder pain, basic arm function, or activities of daily living.

Trial registration

NTR1748.

Keywords

Stroke, upper extremity, muscle stretching exercises, electrical stimulation, activities of daily living, randomized controlled trial.

What is already known on this topic

Contracture of muscles in the arm after stroke is common. Stretch alone does not typically produce clinically important reductions in contracture in people with neurological conditions. Hypertonia may limit the application of stretch and therefore its potential benefits.

What this study adds

In people with poor arm motor control after stroke, static arm positioning to stretch muscles prone to contracture combined with neuromuscular stimulation of the antagonist muscles did not have significant benefits with respect to range of motion, shoulder pain, performance of activities of daily living, hypertonia, spasticity, motor control or shoulder subluxation.

Introduction

Annually, 15 million people worldwide suffer a stroke.[1] About 77–81% of stroke survivors show a motor deficit of the extremities.[2] In almost 66% of patients with an initial paralysis, the affected arm remains inactive and immobilised due to a lack of return of motor function after six months.[3,4] Over time, the central nervous system as well as muscle tissue of the arm adapt to this state of inactivity, often resulting in residual impairments such as hypertonia,[5,6] spasticity[7] or contractures.[7-9] In turn, these secondary impairments are associated with hemiplegic shoulder pain[10,11] and restrictions in performance of activities of daily living.[12,13]

Several interventions improve arm function after stroke and prevent secondary impairments, eg, bilateral arm training[14] or constraint-induced movement therapy.[15] However, these interventions are not suitable for people with severe motor deficits because they require 'active' residual arm motor capacity. For these people 'passive' interventions may be needed to prevent secondary impairments and optimise long-term handling and assistive use of the affected arm. It is also important to elicit muscle activity if at all possible, and to improve arm function. To prevent the loss of passive range of joint motion as a result of contracture of at-risk muscles in the shoulder (eg, internal rotators, adductors) and forearm (eg, pronators, wrist and finger flexors) in particular, the application of arm stretch positioning alongside regular physiotherapy was deemed important,[16] especially because contractures are associated with shoulder pain.[11,17,18] However, in general, passive stretch does not produce clinically important changes in joint range of motion, pain, spasticity, or activity limitations.[19] One explanation for the lack of effect of passive stretch of the shoulder muscles could be the inadequate duration of stretch, with clinical trials using a dose of 20 or 30 minutes only.[20] However, it is questionable whether stretch of the shoulder muscles for much more than 60 minutes per day during intensive rehabilitation programs is feasible.[21]

People with severe motor deficits after stroke have a higher risk of developing increased resistance to passive muscle stretch (hypertonia) and spasticity of the muscles responsible for an antigravity posture.[5,8,22] These muscles are also at risk of developing contracture. As a result, the passive range of the hemiplegic shoulder (exteral rotation, flexion and abduction), elbow (extension), forearm (supination) and wrist (extension) can become restricted.

Stretching hypertonic muscles is difficult when they are not sufficiently relaxed. intervention, can not only be used to improve pain-free range of passive humeral lateral rotation,[24] but also to reduce muscle resistance[25] and glenohumeral subluxation.[24,26] From these results we hypothesised that NMES of selected arm muscles opposite to muscles that are prone to the development of spasticity and contracture might facilitate static arm stretching both through reciprocal inhibition

('relaxation') of antagonist muscles[27-29] and the imposed (cyclic) stretch caused by motor amplitude NMES. Consequently, static arm stretch positioning combined with NMES could potentially result in larger improvements of arm passive range of motion and less (severe) shoulder pain compared to NMES or static stretching alone. From these hypotheses we developed the following research questions:
(1) Does eight weeks of combined static arm stretch positioning with simultaneous NMES prevent the loss of shoulder passive range of motion and the occurrence of shoulder pain more than sham stretch positioning with simultaneous sham NMES (ie, transcutaneous electrical stimulation, TENS) in the subacute phase of stroke?
(2) Does the experimental intervention have any additional effects on timing and severity of shoulder pain, restrictions in daily basic arm activities, resistance to passive stretch (hypertonia) and spasticity, arm motor control, and the degree of shoulder subluxation?

Method

Design

A multicentre, assessor-blinded, randomised controlled trial was conducted. After inclusion, participants were randomised in blocks of four (2:2 allocation ratio) in two strata (Fugl-Meyer Assessment arm score 0–11 points and 12–18 points) at each treatment centre. Opaque, sealed envelopes containing details of group allocation were prepared by the main co-ordinator (LDdJ) before trial commencement. After a local trial co-ordinator had determined eligibility and obtained a patient's consent, the main co-ordinator was contacted by phone. He instructed an independent person to draw an envelope blindfolded and to communicate the result back to the local trial co-ordinator. The local trial co-ordinator then made arrangements for the baseline measurement after which the allocated intervention was initiated. Mid-treatment, end-treatment, and follow-up measurements took place at 4, 8, and 20 weeks after baseline measurement by two independent assessors (physiotherapists), who were unaware of group allocation and not involved in the treatment of participants. To keep the assessors blinded, participants were reminded before each measurement not to reveal the nature of their treatment. Participants were considered to be unaware of group allocation because they were informed about the existence of two intervention groups but not about the study hypothesis. The participants' and assessors' beliefs regarding allocation were checked at the eight-week (ie, end of treatment) assessment using a three-point nominal scale *(I suspect allocation to experimental/control group, I have no clue of group allocation).* All investigators, staff, and participants were kept blinded with regard to the outcome measurements.

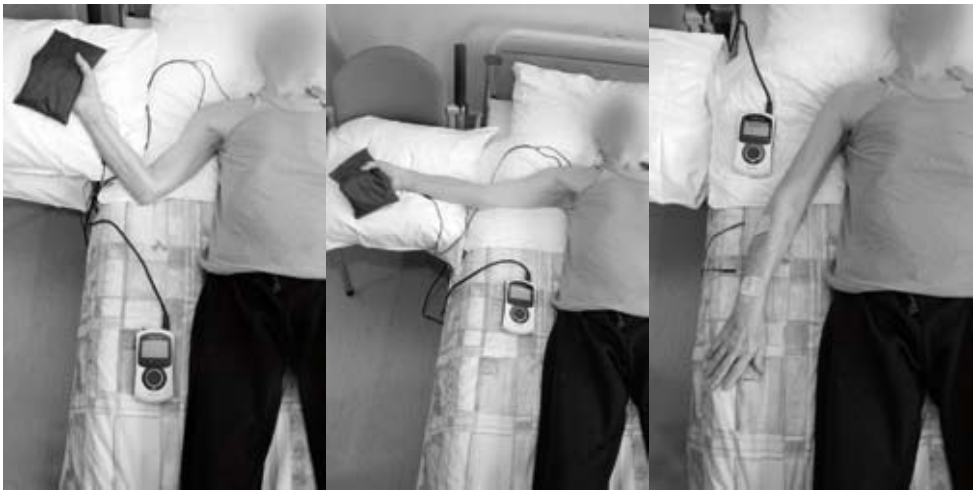
Participants

Between August 2008 and September 2010, consecutive newly admitted patients on the neurological units of three rehabilitation centres in the Netherlands (Beetsterzwaag, Doorn, and Zwolle) were approached for participation. Willing patients were initially screened by a physician for the following inclusion criteria: first-ever or recurrent stroke (except subarachnoid haemorrhages) between two and eight weeks poststroke; age > 18 years; paralysis or severe paresis of the affected arm scoring 1–3 on the recovery stages of Brunnstrom[30]; and no planned date of discharge within four weeks. Subsequently, a local trial co-ordinator excluded patients with: contraindications for electrical stimulation (eg, metal implants, cardiac pacemaker); pre-existing impairments of the affected arm (pre-existing contracture was not an exclusion criterion); severe cognitive deficits and/or severe language comprehension difficulties, defined as < 3/4 correct verbal responses and/or < 3 correct visual graphic rating scale scores on the AbilityQ[31]; and moderate to good arm motor control (> 18 points on the Fugl-Meyer Assessment arm score).

Interventions

All participants received multidisciplinary stroke rehabilitation, ie, daily training in activities of daily living by rehabilitation nurses, occupational therapists, physiotherapists, and speech therapists. These interventions were not standardised, but generally administered in a way that was consistent with the recommendations of the Dutch stroke guidelines.[32] Participants were requested to undergo the additional allocated treatment twice daily for 45 minutes on weekdays for 8 weeks. Participants from the experimental group received arm stretch positioning (presented in Figures 1a and 1b) with simultaneous four-channel motor amplitude NMES. Participants from the control group received a sham stretch positioning procedure (presented in Figure 1c) with simultaneous sham conventional TENS with minimal sensory sensation by using a similar treatment protocol, electrical stimulator and electrode placement (but on the forearm only) as the experimental group. A detailed description of the experimental and control group procedures can be found in Appendix 1.

Treatment was planned to result in 60 hours of positioning and 51 hours of NMES/TENS. All procedures were performed by the local trial coordinator or instructed nursing staff. Nursing staff monitored compliance to the intervention by logging each session on a record sheet, which was always kept in the vicinity of the participant's bed. During the first eight weeks of the trial, prescription of pain and spasticity medication as well as content of physical and occupational therapy sessions for the arm were also monitored.



a b c

Figure 1 Experimental and control arm muscle stretch positions and electrode placements. (a) The intervention used by experimental group participants with sufficient shoulder external rotation to achieve the position. (b) The intervention used by experimental group participants with insufficient shoulder external rotation. (c) The control (ie, sham) intervention .

Outcome measures

The primary outcome measures were passive range of arm motion and pain in the hemiplegic shoulder. All goniometric assessments were performed by two observers using a fluid-filled goniometer (MIE Medical Research Ltd, Leeds, UK) Inter-observer reliability of this technique was high.[33] The presence of shoulder pain was checked using the first (*yes/no*) question of the ShoulderQ.[34] The secondary outcome measures were timing and severity of poststroke shoulder pain, performance of real-life passive and basic daily active arm activities, hypertonia and spasticity, arm motor control and shoulder subluxation. All measurements were carried out in the same fixed order by the same two trained assessors. Every effort was made to motivate participants to undergo all planned measurements even after withdrawal from the study Passive range of shoulder external rotation, flexion and abduction, elbow extesion, forearm supination, wrist extension with extended and flexed fingers were assessed because these movements often develop restrictions in range as a result of imposed immobility, with muscle contractures causing a typical flexion posture of the hemiplegic arm. The (entire) ShoulderQ was administered in participants who indicated that they had shoulder pain. This questionnaire assesses timing and severity of pain by means of eight verbal questions and three vertical visual graphic rating scales. We were primarily interested in the answer to the (verbal) question *How severe is your shoulder pain overall?* (1= *mild*, 2 = *moderate*, 3 = *severe*, 4 = *extremely severe*)

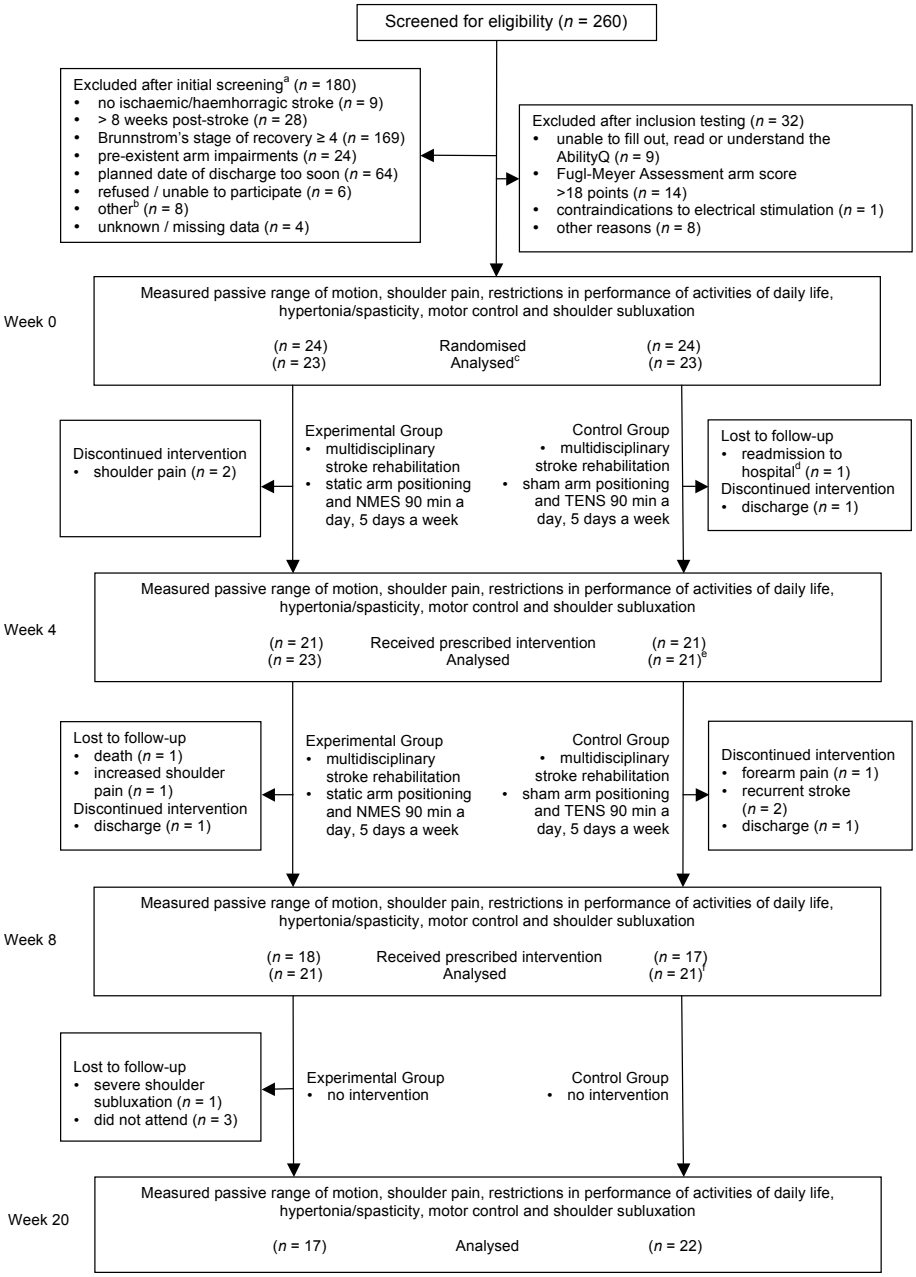


Figure 2 Design and flow of participants through the trial. [a]All reasons for exclusion are listed where patients were ineligible for multiple reasons. [b]Including multiple sclerosis, Alzheimer's disease, locked-in syndrome, recurrent stroke, and participation in another trial. NMES = neuromuscular electrical stimulation. [c]One participant from each group dropped out after randomisation but before receiving any intervention. [d]Unrelated to stroke. [e]One participant missed the Week 4 assessment due to poor weather. [f]One participant missed the Week 8 assessment due to recurrent stroke but was subsequently available for the Week 20 follow-up assessment.

and pain severity measured at rest, on movement, and at night using the 10-cm vertical visual graphic rating scales. The ShoulderQ is sensitive[34] and responsive to change in pain experience.[31] Performance of basic functional activities of daily life involving the passive arm was assessed using the Leeds Adult/Arm Spasticity Impact Scale.[35] Using this semi-structured interview, participants were asked to indicate whether they or their carer(s) experienced difficulty performing 12 different tasks involving the hemiplegic arm (cleaning the palm/elbow/armpits, cutting fingernails, putting the arm through a sleeve/in a glove, rolling over in bed, doing exercises, balancing while standing/walking, and holding objects). The scores on the separate items (1 point = *no difficulty*, 0 = *difficulty or activity not yet performed*) were summed, divided by the total number of items performed and multiplied by 100, resulting in a summary score (0 = *severe disability,* 100 = *no disability*). Hypertonia and spasticity of the shoulder internal rotators, elbow flexors, and long finger flexors were assessed using a detailed version[36] of the Tardieu Scale.[37] The Tardieu Scale can differentiate spasticity from contracture[38,39] and has fair to excellent test-retest reliability and inter-observer reliability.[40] The mean angular velocity of the Tardieu Scale's fast movement was standardised (see Appendix 2). Muscle reaction quality scores ≥ 2 were considered to be clinically relevant hypertonia. Spasticity was deemed present if the angle of catch was present and occurred earlier in range than the maximal muscle length after slow stretching (ie, spasticity angle > 0 degs). Arm motor control was assessed using the 66-point arm section of the Fugl-Meyer Assessment.[41,42] Shoulder inferior subluxation was diagnosed by palpation[43] in finger breadths (< ½, < 1, ≥ 1, > 1½) and considered present if it was one category higher than on the nonaffected side.

Data analysis

Sample size calculation was based on a reliably assessable change in passive shoulder external rotation range of motion of ≥ 17 degs.[33] The clinically relevant difference between the experimental and control intervention was therefore set at a minimum of 20 degs. The standard deviation was considered to be 21.5 degs.[44] Alpha was set at 5% (two-sided), beta at 80%. Thus, the required number of participants in each group was 18. Anticipating a 10% drop-out rate and requiring 36 complete datasets, we aimed to recruit at least 20 participants per group. All participants minus two premature dropouts were analysed as randomised (intention-to-treat). Arm passive range of motion was analysed using a multilevel regression analysis. As main factors time (baseline, 4, 8, and 20 weeks), groupallocation (two groups) and time × group interaction were explored using the –2log-likelihood criterion for model fit, as well as random effects of intercept and slope. For completeness, this analysis was repeated using the data of the

participants including the two premature dropouts (n = 48) using the last observation carried forward approach. Nominal outcome measures (presence of hypertonia/spasticity and subluxation) at eight weeks were analysed using a Chi-square test. Ordinal outcome measures (Fugl-Meyer Assessment, Leeds Adult/Arm Spasticity Impact Scale, ShoulderQ) were first analysed for time effects within subjects using the Friedman test. If differences over time (from baseline to follow-up) were found, these were further explored using the Wilcoxon signed-rank test with Bonferroni-Hochberg correction.[45] Between-group differences were analysed using a Mann-Whitney U test only at 8 weeks to avoid multiple testing.

Results

Flow of participants through the trial

The flow of participants through the trial is presented in Figure 2. Forty-eight patients met all eligibility criteria. One participant from the experimental group (a 68-year-old female with a right-sided ischaemic stroke who regretted participation) and one from the control group (a 62-year old male with a left-sided ischaemic stroke who was rehospitalised due to acute liver-and kidney failure) dropped out the day after baseline measurement and before receiving any intervention. These participants were not included in the analyses because their data were missing due to unavailability for further measurements. Of the 11 patients who were lost to follow-up or discontinued their prescribed intervention during the eight-week treatment period, four (36%) complained of pain. Baseline characteristics of the 46 participants analysed are shown in Table 1. Twenty-two participants (51%, n = 43) had no clue as to which group they were allocated, but 17 participants (40%) were correct in their belief regarding allocation. The three participants who were lost to follow-up before eight weeks did not provide data about allocation beliefs. The two assessors had no clue regarding group allocation in 67% and 72% of the cases. They were correct in their belief regarding allocation in 9 (21%) and 4 (9%) of the participants, respectively.

Co-interventions and compliance with trial method

In the experimental group more participants were prescribed pain and spasticity medication, as presented in Table 2. They also received slightly more conventional therapy for the arm and adhered less to the prescribed intervention protocol. Overall, compliance in the experimental group was 68% (stretch positioning) and 67% (NMES), compared to 78% (sham positioning) and 75% (TENS) in the control group. Non-compliance was mainly caused by drop-out and early weekend leaves. All mentioned differences between the groups were not statistically significant.

Table 1 Baseline characteristics of participants and centres

Characteristic	Exp (*n* = 23)	Con (*n* = 23)
Age (*yr*), mean (SD)	56.6 (14.2)	58.4 (9.6)
Time post-stroke at baseline (days), mean (SD)	43.7 (13.3)	43.3 (15.5)
MMSE[a]: median (IQR)	27 (23 to 28.25)	28 (26 to 29.5)
Gender, n males (%)	15 (65)	12 (52)
Stroke type, n (%)		
ICVA	19 (83)	18 (78)
HCVA	4 (17)	5 (22)
Affected hemisphere, n right (%)	12 (52)	8 (35)
Aphasia, n (%)	5 (22)	6 (26)
Initial FMA arm score, n (%)		
0-11 points	19 (83)	17 (74)
12-18 points	4 (17)	6 (26)
Centres		
Participants treated, n (%)		
Beetsterzwaag	7 (30)	8 (35)
Doorn	4 (17)	4 (17)
Zwolle	12 (52)	11 (48)

Exp = experimental group, Con = control group, FMA = Fugl-Meyer Assessment armscore, HCVA = haemorragic cerebrovascular accident, ICVA = ischaemic cerebrovascular accident, MMSE = Mini Mental State Examination. a Not administered in subjects with aphasia.

Effect of intervention

All primary and secondary outcome measures are presented in Tables 3, 4 and 5. Except for elbow extension and the control participants' wrist extension with extended fingers, both groups showed reductions in mean passive range of motion of all joints (Table 3). The multilevel regression analysis identified significant time effects for the three shoulder movements and for forearm supination. There was no significant group effect nor a significant time × group interaction. A random intercept model fitted the data best (–2log-likelihood criterion). At end-treatment, the mean between-group difference for passive shoulder external rotation was 13 degs (95% CI 1 to 24). At baseline, 37% of all participants (ie, 17/46) reported shoulder pain, as presented in Table 4. At eight weeks, this percentage was 52% (ie, 22/42) with a relative risk of shoulder pain in the experimental group of 1.44 (95% CI 0.80 to 2.62), but no significant difference between the groups (Chi-square = 1.53, p = 0.217). At follow-up 36% (ie, 13/39) of all participants had shoulder pain. At eight weeks, participants with shoulder pain showed no significant between-group differences in their responses to the verbal question as well as in the visual graphic rating scale scores on movement and at night. Overall, the pain scores showed inconsistent

Table 3 Mean (SD) for passive range of motion in degrees for each group, mean (SD) difference within groups, and mean (95% CI) difference between groups. The multi-level regression analysis identified significant time effects for the three shoulder movements and for forearm supination. There was no significant group effect nor a significant group x time interaction. A random intercept results in the best fit for the data (–2log-likelihood criterion).

Outcome	Groups								Difference within groups						Difference between groups		
	Week 0		Week 4		Week 8		Week 20		Week 4 minus Week 0		Week 8 Minus Week 0		Week 20 Minus Week 0		Week 4 Minus Week 0	Week 8 Minus Week 0	Week 20 Minus Week 0
	Exp (*n*=23)	Con (*n*=23)	Exp (*n*=23)	Con (*n*=21)	Exp (*n*=21)	Con (*n*=21)	Exp (*n*=17)	Con (*n*=22)	Exp	Con	Exp	Con	Exp	Con	Exp minus Con	Exp minus Con	Exp minus Con
Shoulder external rotation (deg)	29 (20)	34 (19)	20 (28)	19 (21)	18 (23)	11 (24)	20 (29)	21 (25)	-9 (17)	-14 (14)	-10 (15)	-23 (21)	-5 (23)	-13 (21)	5 (-5 to 14)	13 (1 to 24)	8 (-7 to 22)
Shoulder flexion (deg)	130 (33)	122 (29)	111 (37)	104 (22)	107 (37)	100 (20)	107 (36)	103 (20)	-18 (24)	-15 (18)	-22 (26)	-22 (30)	-16 (31)	-18 (27)	-3 (-16 to 10)	0 (-17 to 18)	2 (-17 to 21)
Shoulder abduction (deg)	110 (48)	93 (41)	93 (51)	71 (32)	92 (51)	66 (27)	84 (46)	72 (27)	-17 (41)	-17 (21)	-18 (48)	-27 (34)	-18 (49)	-20 (33)	0 (-20 to 20)	9 (-17 to 35)	2 (-24 to 29)
Elbow extension (deg)	3 (8)	3 (7)	2 (9)	5 (7)	3 (10)	5 (7)	6 (12)	2 (12)	-1 (6)	1 (5)	0 (8)	2 (7)	2 (8)	-1 (11)	-2 (-5 to 2)	-2 (-7 to 3)	3 (-4 to 9)
Forearm supination (deg)	77 (13)	78 (11)	68 (16)	68 (15)	67 (17)	69 (12)	59 (16)	67 (16)	-8 (12)	-9 (17)	-10 (12)	-9 (12)	-15 (18)	-12 (14)	1 (-8 to 10)	-1 (-8 to 7)	-3 (-13 to 7)
Wrist extension I (deg)	58 (18)	54 (17)	55 (20)	47 (14)	56 (20)	54 (16)[b]	54 (20)	59 (14)	-3 (11)	-5 (12)	-2 (15)	0 (16)[b]	-2 (20)	6 (19)	2 (-5 to 9)	-3 (-12 to 7)	-8 (-21 to 5)
Wrist extension II (deg)	66 (12)	60 (14)	59 (17)[b]	53 (13)	62 (18)	57 (15)	60 (20)	63 (15)	-6 (9)	-6 (8)	-4 (11)	-3 (14)	-4 (16)	3 (15)	0 (-5 to 5)	-1 (-9 to 6)	-7 (-17 to 4)

Exp = experimental group, Con = control group, I = wrist extension with extended fingers, II = wrist extension with flexed fingers. [a] Elbow extension values indicate deviation from the neutral position, ie, degrees of elbow flexor contracture with negative values representing hyperextension. [b]Data missing for one participant.

Table 4 Number of participants per group, medians (IQR) and within- and between-group comparisons of presence of shoulder pain, pain severity scores and visual graphic rating scales of the ShoulderQ[a].

Outcome	Groups								Group comparisons[c]
	Week 0		Week 4		Week 8		Week 20		
	Exp (*n* = 12)	Con (*n* = 5)	Exp (*n* = 10)	Con (*n* = 10)	Exp (*n* = 13)	Con (*n* = 9)	Exp (*n* = 7)	Con (*n* = 7)	
Presence of shoulder pain (*n* and % of group total)	12 (52%)	5 (22%)	10 (44%)	10 (48%)	13 (62%)	9 (43%)	7 (41%)	7 (32%)	X^2: 1.53, p = .217. Relative risk (95%CI): 1.44 (0.80 to 2.62).
Verbal severity score (median and IQR)	1.5 (1 to 2)	2 (2 to 2)	2 (1.75 to 2.25)	2 (1.75 to 2.25)	2 (2 to 3)	2 (1 to 2)	2 (1 to 2)	2 (1 to 2)	Friedman: *n* = 37, X^2 = 11.56, df= 3, *p* = .009. Wilcoxon: sign. change from Week 0 to 8 (z = -2.41, *p* = .016) and Week 8 to 20 (z = -1.98, *p* = .048). Mann-Whitney: *n* = 22, U = 41.5, *p* = .209. Effect size: -.27
VGRS at rest (median and IQR)	1[b] (0 to 3)	3 (0 to 4)	3 (1 to 5)	1.5 (0 to 3)	0.5[b] (0 to 2.5)	2 (0 to 5)	2 (0 to 6)	0[b] (0 to 5.25)	Friedman: *n* = 36, X^2 = 3.27, df = 3, *p* = .351. Mann-Whitney: *n* = 21; U = 41, *p* = .332. Effect size: -.21
VGRS on movement (median and IQR)	5[b] (2 to 6)	4 (2 to 7)	6.5 (5.75 to 8)	4.5 (3 to 6.25)	5[b] (3.5 to 6)	4 (2 to 6.5)	6 (5 to 8)	5[b] (2.75 to 7)	Friedman: *n* = 36,X^2 = 7.97, df = 3, *p* = .047 Wilcoxon: sign. change from Week 0 to 8 (z = -2.102, *p* = .036). Mann-Whitney: *n* = 21; U = 49, *p* = .719 Effect size: -.08
VGRS at night (median and IQR)	1[b] (0 to 3)	4 (3 to 5.5)	3.5 (0.75 to 6.25)	2.5 (1.75 to 5.5)	1[b] (0 to 3.75)	2 (0.5 to 5)	1 (0 to 6)	3[b] (1.5 to4.25)	Friedman: *n* = 36, X^2 = 10.18, df = 3, *p* = .017. Wilcoxon: sign. change from Week 0 to 4 (z = -2.321, *p* = .02). Mann-Whitney: *n* = 21; U = 41, *p* = .345 Effect size: -.21

Exp = experimental group, Con = control group, VGRS = visual graphic rating scale. [a]ShoulderQ verbal severity and VGRS scores were only administered in participants who reported shoulder pain and had the technical ability to answer verbal questions / complete the VGRS scores (as determined by the AbilityQ). The number of participants with pain is presented in the first row of data (ie, presence of shoulder pain). [b]One participant did not have the technical ability to complete the VGRS (but was able to complete the verbal severity score). [c]Between-group comparisons at Week 8 only and Friedman and Wilcoxon tests were performed on full datasets only, allocating a score 0 to those who had no shoulder pain. Mann-Whitney-U-tests were based on data from participants with shoulder pain only.

Table 5 Medians (IQR), number (%) of participants per group and within- and between- group comparisons for performance of daily basic functional arm activities, hypertonia and spasticity (Modified Tardieu Scale), arm motor control (Fugl-Meyer Assessment) and subluxation.

Outcome	Groups								Group comparisons[c]
	Week 0		Week 4		Week 8		Week 20		
	Exp (*n* = 23)	Con (*n* = 23)	Exp (*n* = 23)	Con (*n* = 21)	Exp (*n* = 21)	Con (*n* = 21)	Exp (*n* = 17)	Con (*n* = 22)	
LASIS (median and IQR)	60 (45.5 to 70)	70 (54.5 to 72.7)	63.6 (36.4 to 80)	72.72 (61.8 to 81.8)	72.7[a] (45.4 to 81.8)	77.8 (63.6 to 81.8)	72.7 (61.8 to 80.9)	72.7 (48.9 to 81.8)	Friedman: $n = 37$, $X^2 = 8.62$, df = 3, $p = .035$ Wilcoxon: sign. change from Week 0 to 8 ($z = -2.33$, $p = .02$) Mann-Whitney: $n = 41$, $U = 183.5$, $p = .485$ Effect size: -.11
Elbow flexor hypertonia/spasticity (*n* and within group %)	11 (48%)	10 (44%)	11 (48%)	13 (62%)	11 (52%)	12 (55%)	10 (59%)	14 (64%)	X^2: 0.88, $p = .35$ Relative risk (95%CI): 0.92 (0.53 to 1.59)
Wrist flexor hypertonia/spasticity (*n* and within group %)	16 (73%)[a]	16 (70%)	14 (67%)[b]	15 (71%)	13 (65%)[a]	15 (75%)[a]	12 (75%)[a]	15 (68%)	X^2 : 0.48, $p = .49$ Relative risk (95%CI): 0.87 (0.58 to 1.31)
FMA (median and IQR)	7 (4 to12)	7 (5 to12)	11[a] (4 to 23.75)	12 (5.5 to 27.5)	12 (5 to 29)	10 (5.5 to 27)	19 (7 to 34)	14 (8.5 to 33)	Friedman: $n = 37$, $X^2 = 41.38$, df = 3, $p = <.001$ Wilcoxon: all sign. ($p = <.001$) except Week 4 to 8 ($z = -1.87$, $p = .06$) Mann-Whitney: $n = 42$, $U = 213.5$, $p = .86$ Effect size: -.03
Subluxation (*n* and within group %)	15 (65%)	13[a] (59%)	16 (70%)	10 (48%)	9 (43%)	9[a] (45%)	5 (29%)	7[a] (33%)	X^2 : 0.19, $p = .89$ Relative risk (95%CI): 1.00 (0.50 to 2.01).

Exp = experimental group, Con = control group, LASIS = Leeds Adult/Arm Spasticity Impact Scale, IQR = interquartile range, FMA = Fugl-Meyer Assessment arm score. [a]Data are missing from one participant. [b]Data are missing from two participants. [c]Between-group comparisons at Week 8 only and Friedman and Wilcoxon tests were performed on full datasets only..

Table 2 Mean (SD) or number of participants (%) for co-interventions and compliance to the intervention protocol during the eight-week intervention period and mean difference (MD) or percentage risk difference (RD) between groups, with 95% confidence intervals (95% CI).

Outcome	Groups		
	Exp (*n* = 23)	Con (*n* = 23)	Difference between groups (95% CI)
Prescription of pain medication, *n* (%)	16 (73)[a]	11 (48)	RD 25% (–4% to 50%)
Prescription of spasticity medication, *n* (%)	5 (23)[a]	2 (9)	RD 14% (–8% to 36%)
Upper limb occupational therapy (*hr*), mean (SD)	5 (4)[a]	4 (4)[a]	MD 1 (–2 to 3)
Upper limb physiotherapy (*hr*), mean (SD)	3 (5)	2 (3)[a]	MD 1 (–2 to 3)
Total of positioning (*hr*), mean (SD)	41 (17)[a]	47 (16)	MD-6 (–15 to 4)
Total of electrical stimulation (*hr*), mean (SD)	34 (16)[a]	38 (14)	MD-4 (–13 to 5)

Exp = experimental group, Con = control group. [a]Data missing for one participant.

patterns which hindered within- and between-group comparisons of those with shoulder pain only. There were no significant between-group differences on the Leeds Adult/Arm Spasticity Impact Scale, the Modified Tardieu Scale, the Fugl-Meyer Assessment arm score, and the subluxation scores at end-treatment, as presented in Table 5. It is of note that all participants with clinically relevant hypertonia also demonstrated a spasticity angle > 0 degs and that Tardieu Scale scores for the internal rotators could not be obtained in a large number of participants because they had very limited (< 70 degs) total shoulder external rotation range. The overall prevalence of subluxation decreased from baseline (61%) to follow-up (31%).

Discussion

To our knowledge this is the first study to analyse the effects of a daily arm stretch positioning procedure combined with simultaneous NMES in patients with a poor prognosis for functional recovery in the subacute phase after stroke. The eight-week high-intensity multimodal intervention did not result in any significant differences in arm passive range of motion (contractures), shoulder pain, basic arm activities, hypertonia/spasticity, arm motor control or shoulder subluxation compared to a control group receiving a similar amount of sham positioning combined with TENS in addition to conventional rehabilitation.

Previous attempts to maintain hemiplegic arm joint range of motion using static muscle stretching procedures could not prevent considerable loss of shoulder passive range of motion.[21,44,46,47] Our participants showed similar reductions in mean passive range of motion across most arm joints. Overall, there were no significant differences in passive range of motion between the two groups. At

baseline (on average, six weeks post-stroke), 37% of the participants reported (shoulder) pain. During the intervention period, the prevalence increased to 52% and decreased to 36% three months later. These findings are in line with reports that post-stroke shoulder pain is common, affecting 22–64% of cases, particularly patients with poor arm function.[11,13,48] Overall, pain severity also increased, particularly on movement and at night. This adverse effect was also noted in other trials.[21,46] Although there were no significant between-group differences regarding shoulder pain, worrisome observations were that in the experimental group some participants reported that they considered the intervention to be very arduous, pain and spasticity medication were prescribed more frequently, and protocol compliance was lower. Combined with the finding that shoulder pain was more likely to occur in participants in the experimental group than in the control group (relative risk 1.44), these findings may indicate that for some participants the experimental procedure was not well tolerated.

During the eight weeks of intervention our participants showed increased Leeds Adult/Arm Spasticity Impact Scale sum scores and Fugl-Meyer Assessment arm motor scores, changes that were probably not clinically relevant and caused by a mix of spontaneous post-stroke recovery of function, learned capacity to use compensatory movement strategies of the nonaffected arm and/or increased involvement of the carer. Overall, the prevalence of elbow flexor hypertonia and spasticity jointly increased up to 55% at the end of the treatment period, roughly corresponding to three months post-stroke for our participants. These results are in concordance with previous work.[5,6,22] The unexpected high prevalence of hypertonia and spasticity (62%) and a decreasing prevalence of shoulder subluxation (31%) at follow-up in our sample may be explained by the fact that patients with relatively poor arm motor control have a higher risk of developing hypertonia.[5]

Although we performed an intention-to-treat analysis (ie, using any available data from all randomised subjects), we did not use forward imputation of missing data representing a clinical variable (eg, shoulder passive range of motion) that is worsening over time,[17] as this might increase the chance of a Type I error. However, for completeness, this stricter intention-to-treat analysis using the data of all randomised subjects (n = 48) was performed. This analysis was similar in outcome to the original analysis but revealed an additional time effect of wrist extension with flexed fingers. A per protocol analysis would also have resulted in similar results because no patients crossed over to the other group. We also refrained from performing a sensitivity analysis based on compliance because

meaningful conclusions could not be drawn from the resulting limited sample sizes. We furthermore acknowledge that the Leeds Adult/Arm Spasticity Impact Scale lacks psychometric evaluation and our method to standardise the Tardieu Scale's stretch velocity (V3) using a metronome was not validated and tested for reliability. Therefore, our data regarding basic arm activities, hypertonia, and spasticity should be interpreted with caution. Finally, because overall compliance to both protocols was only about 70%, an underestimation of the treatment effect may also have occurred. Nevertheless, the combined administration of 43 hours of static stretching and 36 hours of NMES was more than administered during any previous trial.[20]

A recent study produced inconclusive evidence about the effectiveness of a combined intervention of electrical stimulation in conjunction with prolonged muscle stretch (using a splint) to treat and prevent wrist contracture.[49] Similarly, our results also showed no added benefit of electrical stimulation during static stretching of the shoulder and arm. The results of these multimodal approaches to the problem of post-stroke arm contracture development are in line with the conclusion of a review[19] that static stretch positioning procedures have little, if any, short or long term effects on muscle contracture (treatment effect ≤ 3 deg), pain, spasticity, or activity limitations. Although pooled data from studies investigating the effects of electrical stimulation suggested some treatment effects on functional motor ability[26] and pain-free range of passive humeral lateral rotation in patients with residual arm motor capacity,[24] we found no such results in our sample of patients without residual arm motor capacity. As the combined procedure did not result in any meaningful treatment effects, it suggests that application of muscle stretching or NMES alone as a monotherapeutic intervention will not have a clinically relevant impact in this subgroup of patients either.

Research to date suggests that it is not possible to control or overcome (the emergence of) contractures and hypertonia using the current static arm muscle stretching procedures. Similarly, NMES of the antagonists of the muscles prone to shortening does not seem to provide additional benefits either. We therefore argue that these techniques should be discontinued in the treatment of patients with a poor prognosis for functional recovery. In this subgroup of patients it is becoming an increasingly difficult challenge to find effective treatments that can prevent the development of the most common residual impairments such as contractures, hypertonia, and spasticity and its associated secondary problems such as shoulder pain and restrictions in performance of daily life activities. Further research is required to investigate what renders these interventions ineffective. The

efficacy of other approaches, such as transcranial magnetic stimulation, NMES of the muscles prone to shortening,[50] or other combinations of techniques, could also be investigated.

Ethics

The study was approved by the Medical Ethics Committee of the University Medical Center Groningen. All participants gave written informed consent prior to participation.

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Competing interests

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Appendix 1
Details of intervention method

Experimental group
The aim of the electrical stimulation was to enhance the mobilising effect of the static positioning procedure, i.e. to mobilise the wrist to pure wrist (≤ 20 degrees) and finger extension (stretching the wrist and finger flexors) and to mobilise the shoulder to external rotation, horizontal extension and slight abduction (stretching the internal rotators, flexors and adductors). First, electrodes were placed over the motor point of the extensor digitorum communis muscle and the dorsal surface of the distal forearm. Two other electrodes were placed over the dorsal surface (pars posterior) of the deltoid muscle and over the infraspinatus/teres minor muscle(s). The electrical stimulator (STIWELL-med4, Otto Bock HealthCare, Germany) was programmed to deliver a symmetric bi-phasic wave pattern of 35 Hz and a pulse width of 300µs. Stimulation on and off time was 8 seconds with a 3 second ramp-up and ramp-down. For skin adaptation purposes the stimulation time was gradually increased from 10 to 45 minutes per session (with increments of 5 minutes every other day) during the first 13 days. Amplitudes never exceeded the individual's comfort level and skin checks were performed after every session. After electrode placement, the arm was carefully positioned in maximally available pain-free shoulder abduction and external rotation while avoiding impingement of the rotator cuff muscles. Because of individual differences in PROM, the position of the arm varied (Figure 1a and 1b). To keep the fingers and wrist in a neutral position, the forearm supinated and to pull the shoulder into external rotation, a sandbag (± 0.5 kg) was placed on the volar surface of the hand. Participants were instructed not to change the position of the arm or trunk during treatment.

Control Group
The basic stimulation (80Hz, pulse width 150µs) was just above the participants' sensation threshold, giving no muscle contraction but a tingling sensation at the most. Subsequently, the affected arm was positioned in shoulder internal rotation and ≤ 30 degrees of abduction (Figure 1c).

Appendix 2

Tardieu Scale[1] terminology and measurement procedure

Terminology:[2]

Velocity to stretch (V):

V1: As slow as possible.

V2: Speed of the limb segment falling under gravity.

V3: As fast as possible (faster than the rate of the natural drop of the limb under gravity).

Only V2 and V3 are used to rate spasticity

For each muscle group, reaction to stretch was rated at the specified stretch velocity with two parameters X and R.

Quality of muscle reaction (X):

0: No resistance throughout the course of the passive movement.

1: Slight resistance throughout the course of the passive movement, with no clear catch at a precise angle.

2: Clear catch at a precise angle, interrupting the passive movement, followed by release.

3: Fatigable clonus (< 10 seconds when maintaining pressure) occurring at a precise angle.

4: Infatigable clonus (> 10 seconds when maintaining pressure) occurring at a precise angle.

Angle of muscle reaction (R):

R1: angle of 'catch', resulting from overactive stretch reflex.

R2: angle of the muscle length at rest.

The difference between R2 and R1 is the *spasticity angle.*

Measurement procedure

First, moving "as slow as possible" (V1) the total passive range of motion ($PROM_{max}$) of the actual joint was determined, including the muscle length at rest (R2). The standardized mean angular velocity (ω) of the fast movement (V3) was 300°/s[3] using a metronome to convert this velocity into an audible signal for the observers. Because each subject has a different $PROM_{max}$, the individual movement frequency (in beats per minute) had to be calculated (movement frequency = (ω / $PROM_{max}$) × 60). Participants with < 70° total shoulder joint rotation range (≥ 249 bpm on the metronome) were not assessed because of the imminent risk of injury at higher movements speeds. Joint ranges were clustered in groups of five degrees and corresponding beats per minute were rounded to their middle value (e.g. 70°-75°

at 257-240 bpm = 249 bpm). If applicable, one observer moved the joint through range (starting the movement on one click and ending it on the next) and rated the quality of the muscle reaction to stretch (X). The other observer assessed the 'angle of catch' (R1) if it occurred. Grading was performed in a constant position of the body for the given joint. Other joints were kept in the same position throughout the test and between tests.

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Chapter 5

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The hemiplegic arm: interrater reliability and concurrent validity of passive range of motion measurements

Disability and Rehabilitation. 2007;29(18): 1442-1448

Abstract

Purpose

To assess whether our measurement protocol using two raters simultaneously yielded reliable passive range of motion measurements of the hemiplegic arm. Additionally, motion ranges were correlated to several factors to examine the concurrent validity of these measurements.

Method

Two raters simultaneously assessed five arm motions at baseline, after five and ten weeks in respectively 18, 13 and 12 stroke patients. One tester made the passive movement and the other read the hydrogoniometer. Raters then switched roles.

Results

Intraclass correlation coefficients (ICCs) revealed high agreement between the raters with ICCs ranging between 0.84 and 0.99. Standard errors of measurement and smallest detectable differences were large for shoulder abduction. Significant correlations were found between shoulder external rotation and flexion. All arm motions correlated negatively to pain at the end range of these motions. Shoulder external rotation and flexion were significantly correlated to the time poststroke. Concurrent validity with Ashworth Scale, Fugl-Meyer Assessment and Barthel Index was limited.

Conclusions

The current measurement protocol yielded high reliability indices and seems useful for further use. However, standard error of measurement and smallest detectable difference for shoulder abduction were high, implying the neccesity to include a large sample size in future studies. Correlations revealed that restricted range of arm motions relate to the time poststroke and coincide with pain.

Keywords

Cerebrovascular accident, upper extremity, range of motion, reproducibility of results.

Introduction

Limitations in functions and activities of the hemiplegic arm are well known phenomena for those involved in the rehabilitation of stroke patients. Despite the fact that hemiplegic shoulder pain receives extensive attention in the literature, as expressed by a large number of recent articles and reviews,[eg. 1-3] it seems clear that it is still a long way before the most optimal combination of treatment modalities is found.

One of the most commonly used outcome measures in upper limb rehabilitation are active and passive range of motion (ROM), using (several types of) goniometers. Overall conclusions from the available reports indicate that range ofmotion measurements in healthy subjects and in patients with (most) orthopaedic conditions in the shoulder and elbow joint can be highly reliable, both within testers and slightly less between testers if some specific conditions are met.[4-8] Less, however, is known about the reliability of the measurements in neurological conditions such as stroke. Especially information concerning passive range of motion (PROM) measurements of the hemiplegic limb is scarce. This may have to do with the fact that it is difficult to assess range of motion of a limb that is more or less paralysed and in some cases resists passive movement as a consequence of spasticity and contractures. In addition to these problems, many stroke patients suffer from hemiplegic shoulder pain, a condition closely related to restricted range of motion.[9,10] Using only one rater during PROM measurements under these conditions might introduce serious measurement errors, since it is difficult to handle the hemiplegic limb and goniometer and reading the score all simultaneously.

Despite the presumption that aforementioned factors may limit a reliable assessment, reliability of PROM measurements in stroke patients was shown to be good for the shoulder joint with respect to lateral rotation.[11] However, when it comes to measurements of motions other than shoulder external rotation or the assessment of the elbow and forearm joints, information is lacking.

As part of a randomized clinical trial into the effectiveness of a contracture preventive positioning procedure for the involved upper limb in stroke patients[12] we explored the interrater reliability of our PROM measurements. This study addressed the question whether PROM measurements were reliable when using a standardised measurement protocol. Since previous studies revealed relationships between passive joint range of motion and both pain and time poststroke, we additionally explored whether the baseline range of motion measurements had mutual correlations or correlated with pain scores, the time since onset of the stroke, resistance to passive stretch ('spasticity') as reflected by Ashworth Scale grades, the ability to make selective arm movements using the arm section of

the Fugl-Meyer Assessment and performance of activities of daily life (ADL) as reflected by the Barthel Index. Correlating these measures might be helpful in revealing factors associated with range of motion measurements as indicators of their concurrent validity.

Method

Subjects

Subjects were selected from three rehabilitation centres in the Netherlands (Apeldoorn, Doorn and Zwolle). All stroke patients admitted between March 2003 (one centre participated as from January 2004) and January 2005, were initially screened by a physician. Subjects had to meet the following inclusion criteria: (1) First ever stroke as defined by the World Health Organization[13] and maximally 12 weeks poststroke; (2) a medial cerebral artery stroke, established by means of CT/MRI; (3) no premorbid impairments of the affected upper limb; (4) no severe shoulder pain during passive arm motions as subjectively judged by the physician; (5) no use of antispasticity drugs; (6) no use of pain reducing drugs except for Paracetamol, (7) no planned date of discharge and (8) able to give written informed consent. Subjects with fair to good involved upper limb recovery (as defined by Brunnstrom's stages of recovery 4, 5 or 6[14] as judged by the physician) were excluded. Patients who met the inclusion criteria were then referred to a physiotherapist, who administered tests to exclude patients with (9) severe neglect (a difference of more than three O's on the letter cancellation test),[15] severe loss of position sense (scores 2 and 3 on the Thumb Finding Test[16-18]) and cognitive impairment scoring lower than 23 points on the Mini Mental State Examination.[19-21] Subjects with aphasia who could not answer the questions of the Mini Mental State Examination were tested by means of the language comprehension sub-items of the Akense Afasie Test[22] (minimum 67 points). Finally, patients who were able to prevent contracture by producing voluntary movement, having a Fugl-Meyer Assessment arm score[23] of more than 18 points on the subscales for shoulder- and elbow motions, were excluded. The study All subjects gave written informed consent prior to participation.

Raters

Two raters, both physiotherapists, had 7 and 4 years of experience, respectively, with the treatment of stroke patients. Before the trial, raters received and studied a detailed, unpublished manual of a measurement procedure written for the sole purpose of this study. Subsequently, both raters received a standardised pre-trial training in administering the PROM measurements and practiced it on three stroke patients. Raters had no pre-trial experience using the hydrogoniometer and were

not involved in the design of the study or the treatment of the patients during the main trial.

Measurement procedure for PROM measurements and pain scores

All PROM measurements were performed using a masked fluid-filled (hydro) goniometer (MIE Medical Research Ltd., Leeds, U.K.). A hydrogoniometer was found to be a reliable tool in quantifying ROM,[11,24,25] probably due to the fact that the starting position of this type of goniometer can be consistently identified and repeated since gravity does not change.[26] To ensure standardization of the PROM testing procedures the raters were trained beforehand,[6,27] shoulder abduction was applied during several shoulder motions,[5,11,27] and the two raters worked in pairs; one rater performed the passive motion and the other aligned and read the hydrogoniometer.[28] The measurement protocol furthermore entailed the following procedures and rules: Before the actual measurement, each joint-motion was performed through the full range as a connective tissue 'warm-up'. The movement speed of each measurement was at least 2 sec for the entire available range in order to make sure no stretch reflex ('spasticity') was elicited. Both raters were instructed to check for and prevent compensatory movements of the subject's head or trunk that could influence the actual measurement.

The measurements of PROM of five arm motions were carried out as follows: the first rater carried out the 'warming up' and the actual passive movement. The second rater measured the maximum range with the hydrogoniometer. The value representing the lowest point of the column of fluid was noted with an accuracy to 1 degree. The second rater asked the subjects to report pain at the end feel of each passive motion (0 = no pain, 1 = pain). The second rater was instructed not to look at the hydrogoniometer while performing the motion despite the fact that the backside of the hydrogoniometer was opaque, and not to look at the rater while noting the score on the scoresheet. Then, the raters changed roles and the procedure was repeated only checking for, but not scoring pain. Measurement sequence was as follows: shoulder flexion, shoulder external rotation and elbow extension in supine, followed by shoulder abduction and forearm supination in sitting on an adjustable massage table with the back supported. The same two raters, who carried out all the measurements in the same fixed order, were blinded to each other's results by using separate score sheets and were furthermore instructed not to discuss or mention the values found.

Statistical Analyses

Interrater reliability of the PROM measurements was calculated by means of intraclass correlation coefficients (3,1) on data produced from a two-way analysis

of variance (ANOVA)[29] with consistency mode. The reason for choosing this type of intraclass correlation coefficient (ICC) was that the testing was only to be performed by two and the same raters for the purposes of assessing the reliability of the measurements for the main trial. Because an ICC alone gives no indication of the magnitude of disagreement between the raters, standard error of measurement (SEM) was calculated additionaly using the formula $sd \times \sqrt{(1-r)}$. The smallest detectable difference (SDD) was calculated using the formula $1.96 \times \sqrt{2} \times SEM$. To prevent dependency in the data, the ICC-values were calculated for three different datasets, representing the three different evaluation moments of the main trial (baseline-, five and ten week measurements). Due to subject dropout from the main trial (as a result of illness, the administration of botulinum toxin/pain medication or discharge) and the absence of one of the raters, ICCs for respectively 18, 13 and 12 subjects could be calculated. Mutual PROM correlations and correlations between motion range and the onset of stroke were calculated by means of the Pearson correlation coefficient. Correlations between the ratio-level PROM scores and the dichotomous pain score would require a point-biserial correlation coefficient. Since this correlation is equivalent to computing the Pearson correlation and is interpreted similarly, correlations between the different arm motions and painscores at the end range of these motions, Ashworth Scale gradings, Fugl-Meyer Assessment scores and Barthel Index scores were all calculated by means of the Spearman correlation coefficient. Correlation coefficients were calculated using baseline data only. All statistical procedures were carried out using SPSS for Windows (version 10.0.5).

Results

The included ten men and nine women had a mean (±SD) age of 54 (±10) years and were 39 (±12) days poststroke during the first evaluation. Most subjects suffered an ischaemic stroke (n = 14) and the side of hemiparesis was divided nearly equally over all subjects. The median score of the upper-extremity section of the Fugl-Meyer Assessment was 10 out of a maximum of 66 points, implying that the participating subjects had very poor recovery of active arm movement capability. The subjects' baseline PROM for shoulder external rotation ranged between 15 and 94 degrees, shoulder flexion between 87 and 180 degrees, shoulder abduction between 65 and 104 degrees, elbow extension between 72 and 116 degrees and forearm supination between 25 and 99 degrees. Tables IA, IB and IC present the different values of the evaluations for the 18, 13 and 12 subjects at baseline, after five- and ten weeks, respectively. Overall the ICCs ranged between 0.78 and 0.99. The smallest detectable difference varied between 6 and 19 degrees of which the shoulder abduction measurements never reached values lower than 11 degrees. Table II shows that, in addition to a high positive correlation between the range of

Table I (A-C) Intraclass correlation coefficients (ICCs; 95% confidence interval, 95% CI), standard error of measurement (SEM) and smallest detectable difference (SDD) of passive range of motion (PROM) measurements between the two raters at (A) baseline, (B) five and (C) ten weeks.

Variable	ICC	95% CI	SEM	SDD
(A)				
		At baseline (*n* = 18)		
Shoulder external rotation	0.94	0.85-0.98	3.05	8.45°
Shoulder flexion	0.98	0.95-0.99	3.60	9.98°
Shoulder abduction	0.84	0.62-0.94	4.32	11.97°
Elbow extension	0.78	0.49-0.91	4.86	13.47°
Forearm supination	0.94	0.85-0.98	4.42	12.25°
(B)				
		At five weeks (*n* = 13)		
Shoulder external rotation	0.97	0.91-0.99	3.53	9.78°
Shoulder flexion	0.99	0.97-0.99	3.00	8.31°
Shoulder abduction	0.87	0.64-0.96	5.94	16.46°
Elbow extension	0.94	0.81-0.98	2.59	7.18°
Forearm supination	0.95	0.84-0.98	4.18	11.58°
(C)				
		At ten weeks (*n* = 12)		
Shoulder external rotation	0.99	0.97-0.99	2.42	6.71°
Shoulder flexion	0.98	0.94-0.99	4.56	12.64°
Shoulder abduction	0.84	0.54-0.95	6.54	18.13°
Elbow extension	0.97	0.91-0.99	2.32	6.43°
Forearm supination	0.98	0.92-0.99	3.02	8.37°

SDD in degrees (°).

shoulder external rotation and shoulder flexion (r = 0.731, p = 0.01), all motions were negatively correlated to pain at the end of that particular motion. Shoulder abduction and forearm supination however were only moderately correlated to pain at the end range of motion (r = 0.456 and 0.459, p = 0.05). Shoulder flexion was furthermore negatively correlated to pain at the end of the four other motions and shoulder external rotation to pain at the end range of shoulder flexion and elbow extension. The passive range of shoulder external rotation and flexion were correlated to the time poststroke, albeit only at the five-percent significance level for the shoulder flexion. Furthermore, shoulder flexion was moderately correlated to the ability to make selective movements of the hemiplegic arm as assessed by the Fugl-Meyer Assessment and elbow extension was highly correlated to the independence in ADL as measured by means of the Barthel Index.

Table 2 Correlations between hemiplegic arm passive range of motion (PROM) and pain at the end range of motion, time since onset of stroke, resistance to passive stretch of the elbow flexors (Ashworth Scale), the ability to make selective arm movements (Fugl-Meyer Assessment, arm section) and activities of daily life (Barthel Index).

			PROM		
	Shoulder external rotation	**Shoulder flexion**	**Shoulder abduction**	**Elbow extension**	**Forearm supination**
PROM					
Shoulder external rotation					
Shoulder flexion	0.731**				
Shoulder abduction	0.056	0.356			
Elbow extension	0.391	0.380	0.117		
Forearm supination	0.306	0.355	-0.064	0.005	
Pain					
Shoulder external rotation	-0.618**	-0.459*	-0.419	-0.329	-0.339
Shoulder flexion	-0.655**	-0.622**	-0.044	-0.055	-0.219
Shoulder abduction	-0.372	-0.559*	-0.456*	-0.124	-0.104
Elbow extension	-0.478*	-0.628**	-0.060	-0.688**	-0.010
Forearm supination	-0.438	-0.598**	-0.150	-0.060	-0.459*
Time poststroke	-0.595**	-0.483*	-0.280	0.188	-0.454
Ashworth Scale	0.098	0.041	0.296	-0.207	0.157
Fugl-Meyer Assessment	0.174	0.467*	-0.108	0.336	0.033
Barthel Index	0.151	0.143	-0.158	0.592**	0.063

*Correlation significant at the 0.05 level (2-tailed);
**correlation significant at the 0.01 level (2-tailed).

Discussion

The aim of this study was to investigate whether a standardized range of motion measurement protocol, using two raters simultaneously, would yield reliable measurements for five different passive motions of the hemiplegic arm. When classifying the ICC values as suggested by Portney and Watkins[30] (≥ 0.75 high reliability, 0.40-0.75 moderate reliability, ≤ 0.40 poor reliability) the conclusion is justified that the overall interrater reliability of our measurement protocol was high. Standard error of measurement however varied between the three different evaluations, but was high for shoulder abduction on all occasions. The use of small sample sizes probably contributed to these high indices. Furthermore, passive shoulder external rotation and flexion were highly correlated. All five arm motions were correlated to pain at the end range of these motions. Shoulder external rotation and flexion were correlated to pain at the end range of nearly

all other motions and were also significantly correlated to the time post stroke. Although shoulder flexion was moderately and negatively correlated to the Fugl-Meyer Assessment and elbow extension was highly correlated with the Barthel Index, concurrent validity of these measures with range of motion measurements seemed limited.

Comparison of our results with other studies on interrater reliability of PROM of the arm[5,8,31-35] is hampered by differences in measurement protocols, including different goniometers, subjects, positions and observers. Our testing procedure mostly resembled the procedure used by Andrews and Bohannon,[11] who found an interrater ICC of 0.96 for shoulder lateral rotation on the paretic side using 25 stroke patients. During our three different evaluations of respectively 18, 13 and 12 subjects we found comparable ICCs of 0.94, 0.97 and 0.99. This finding suggests that using two raters simultaneously instead of one does not result in more reliable measurements when assessing shoulder external rotation. However, we also assessed passive shoulder abduction and flexion. Especially these two movements could be difficult to measure by just one rater as the hemiplegic limb and goniometer have to be handled and read at the same time. Despite our hypothesis that two pairs of hands would yield more reliable measurements, shoulder abduction assessments clearly revealed lower ICCs than the other motions (maximum .87), although these values can still be considered high. Clearly, using two raters did not induce higher reliability indices on all occassions. In addition, from a rehabilitation practitioner's point of view, it can be argued that using two pairs of hands is not always feasible when assessing range of motion. Nevertheless, our measurement protocol can still be useful for other motions than shoulder external rotation and for scientific purposes using stroke patients.

One other major limitation of this study is the use of small sample sizes during the three different evaluations. Small sample sizes will yield an imprecise estimate of the reliability coefficients which is indicated by an excessively wide confidence interval.[36] As a consequence, standard error of measurement increases. Standard errors of measurement found by MacDermid et al.[5] indicated that differences of approximately 5-7 degrees could be attributable to measurement error within raters and somewhat greater between raters. Our standard errors of measurement varied between 2 and 7 degrees, confirming this range for stroke subjects.

The smallest detectable difference (SDD) is another important index that may give therapists or scientists information as to whether a difference measured is due to random measurement error or actually represents a true change in the

patients PROM. Values generated during this trial showed that the SDD for the five different arm motions during the three different evaluations ranged between 6 and 19 degrees. The minimum difference of, e.g., shoulder external rotation that needs to be exceeded to be reasonably certain that a real change has occurred was found to be 10 degrees. Applied to the other motions, the differences for shoulder flexion and forearm supination would have to be 13 degrees, 14 degrees for elbow extension and 19 degrees for shoulder abduction. These rather large SDD's are probably caused by the use of the small sample sizes during the three different evaluations. The variation of smallest detectable differences between the five motions may reflect the number of degrees of freedom of the different joint motions; the more degrees of freedom, the harder they are to control. Compensatory movements of the trunk during shoulder abduction may therefore have contributed to larger measurement errors, and hence lower ICCs. On the other hand, the findings were replicated during three consecutive evaluations, which seem to support the robustness of the findings. Nevertheless, the SEM and SDD results imply the necessity to include a large sample size in future studies.

Of all five motions tested, shoulder external rotation and flexion were most highly correlated (.731, $p = 0.01$). Restrictions of shoulder external rotation usually coincide with a decrease of glenohumeral flexion since elevation in all planes anterior to to the scapular plane require external axial rotation of the humerus.[37] Contracture of shoulder connective tissue or hypertonus of shoulder muscles may have enhanced this relationship. Baseline data revealed that of all participating subjects the passive range of external rotation was restricted for approximately 50% and flexion for approximately 25% of the normal range (data published elsewhere[12]). The highly significant correlation combined with this 2:1 ratio could be used to clinically estimate the decrease of shoulder flexion on the basis of knowledge of the shoulder external rotation range of motion. However, this ratio needs future verification.

Each range of motion was significantly and negatively correlated with pain at the end range of that same particular motion. This is more or less in concordance with previous work,[9,10,38-40] although the methods of assessment of PROM and pain varied between these different studies. In addition, shoulder flexion and (to a lesser extent) external rotation were correlated to pain at the end range of nearly all other motions.

This 'passive-motion-range-and-pain' relationship, found in this and previous studies, once again shows that it is highly likely that one month post stroke

hemiplegic arm motions are restricted and painful. Similar to the findings of Andrews and Bohannon[11] and Bohannon et al.,[9] we found a positive relationship between shoulder external rotation on the paretic side and time since onset of stroke. In our study, this relationship was also moderately high for shoulder flexion (r = 0.483, p = 0.05). These relationships make it clear that the amount of time passed since the onset of a stroke closely relates to a decrease in hemiplegic arm range of motion. This may be caused by gradual contracture formation. Decreased PROM of the arm joints, in turn, is related to pain at the end range of these motions, although, the cause of the developing pain is thought to be multifactorial.[2]

The passive shoulder flexion correlated moderately to the Fugl-Meyer Assessment scores. Since reductions in arm motion ranges affect this motor score, this finding was not surprising. It was surprising, however, to find that the correlation was only significant for shoulder flexion, a result which is difficult to interpret. Finally, passive elbow extension was correlated to independence in ADL, which is also difficult to explain since the Barthel Index only assesses functional activities and does not take arm motion ranges into account.

Although we established the reliability of measurements using two independent raters only, our measurement protocol seems to be of use for other raters under comparable circumstances. Trials with larger samples of stroke subjects should reveal if using two raters simultaneously yields higher reliability indices than only a single rater for arm movements other than shoulder external rotation. Given the low correlations of the range of motion measurements with the Ashworth Scale, Fugl-Meyer Assessment and the Barthel Index, the concurrent validity of the range of motion measurements seems to be limited. The correlation with the time poststroke indicates the importance of early intervention strategies aimed at preventing loss of range of motion in the hemiplegic arm.

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Chapter 6

Lex D. de Jong | Pieter U. Dijkstra | Roy E. Stewart | Klaas Postema

Repeated measurements of arm joint passive range of motion after stroke: interobserver reliability and sources of variation

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Abstract

Background

Goniometric measurements of hemiplegic arm joints must be reliable to draw proper clinical and scientific conclusions. Previous reliability studies were cross-sectional and based on small samples. Knowledge about the contributions of sources of variation to these measurement results is lacking.

Objective

The aims of this study were to determine interobserver reliability of measurements of passive range of motion (PROM) over time, explore sources of variation associated with these measurement results, and generate smallest detectable differences for clinical decision making.

Design

This investigation was a measurement-focused study with a longitudinal design, nested within a two-arm randomized controlled trial.

Methods

Two trained physical therapists assessed seven arm movements at baseline and after 4, 8, and 20 weeks weeks in 48 people with subacute stroke patients using a standardized protocol. One physical therapist performed the passive movement, and the other read the hydrogoniometer. The therapists then switched roles. The relative contributions of several sources of variation to error variance was explored with analysis of variance.

Results

Interobserver reliability coefficients ranged from .89 to .97. The PROM measurements were influenced by error variance ranging from 31% to 50%. The participant x time interaction made the largest contribution to error variance, ranging from 59% to 81%. Smallest detectable differences were 6 to 22 degrees and were largest for shoulder movements.

Limitations

Verification of shoulder pain and hypertonia as sources of error variance led to a substantial number of unstable variance components, necessitating a simpler analysis.

Conclusions

The assessment of PROM with a standardized protocol, a hydrogoniometer, and two trained physical therapists yielded high interobserver reliability indexes for all arm movements. Error variance made a large contribution to the variation in measurement results. The resulting smallest detectable differences can be used to interpret future hemiplegic arm PROM measurements with more confidence.

Introduction

Of the 15 million people who have a stroke each year worldwide, between 77% and 81% of the survivors have a motor deficit in the extremities.[1] The affected arm remains without function in almost 66% of survivors,[2,3] rendering it inactive and immobilized. In recent years, several interventions believed to improve motorrecovery or limit development of secondary impairments in the paretic or paralyzed arm after stroke have been evaluated.[eg. 4,5]

To assess the arm function of patients with stroke during rehabilitation and in clinical research, physical therapists regularly assess passive range of motion (PROM) of joints by means of goniometry. In particular, the degree of passive shoulder external rotation and abduction and wrist extension are commonly used as outcome measures to evaluate the effects of interventions.[6-13] Reliable measurement of PROM is therefore an important prerequisite for the interpretation of study results. The reliability of arm range-of-motion measurements is good in people who are healthy[14,15] and in patients with orthopedic conditions,[16,17] but these findings cannot be generalized to patients with stroke because stroke-specific impairments may influence reliability. Over time, many patients develop contractures[10,18] and hypertonia,[19,20] especially in shoulder internal rotators and wrist flexors. Many patients also develop shoulder pain, a condition strongly associated with restricted range of motion.[21,22] The aforementioned factors may hinder the therapist's attempts to move the hemiplegic arm, hence increasing the chance of making measurement errors. Such errors also may be increased if PROM measurements are obtained by only one therapist because it is difficult to handle a paralyzed arm and the goniometer and read the measurement simultaneously. Goniometric measurements of arm joints reflect both the true range of a joint and measurement errors caused by different sources of variation. Identifying and quantifying these sources are important for finding strategies to reduce their influence on outcomes.[23] In addition, to ensure accurate clinical interpretation of joint PROM measurements and changes in these measurements over time during poststroke rehabilitation or research, PROM measurements should be studied in the context of these sources of variation. In previous studies of arm PROM reliability in patients with stroke, sample sizes have not exceeded 18 people.[24,25] To our knowledge, research into factors that may influence hemiplegic arm PROM measurements is also lacking. During a randomized controlled trial,[26] two physical therapists (hereafter referred to as 'observers') assessed arm joint PROM in 48 people on four occasions over 20 weeks. This design presented us with the opportunity to explore interobserver reliability, analyze the contributions of sources of variation to the measurement results, and calculate smallest detectable differences (SDDs). We chose to use two observers because we hypothesized that

doing so would result in fewer measurement errors than using one observer only and because a similar measurement procedure previously yielded high reliability indices.[25]

Method

As part of a randomized clinical trial investigating an arm intervention for people with subacute stroke and poor arm recovery, we used an existing measurement protocol that was specifically designed for measuring the PROM of seven arm movements. All participants gave written informed consent before participation.

Participants

Participants were recruited from three Dutch rehabilitation centers between August 2008 and September 2010. All admitted participants were initially screened by a physician to check the following inclusion criteria: first-ever stroke or recurrent stroke (except for subarachnoid haemorrhages) between two and eight weeks after the initial stroke, age of 18 years or older, paralysis or severe paresis of the involved upper limb (Brunnstrom stage of recovery of < 4,[27] as judged by the physician) and no planned date of discharge within four weeks. Participants meeting these criteria were referred to a research physical therapist, who excluded those with any contraindications for electrical stimulation, preexisting impairments of the affected arm (eg, frozen shoulder), severe cognitive deficits or severe language comprehension difficulties or both (<3/4 correct verbal responses and/or <3 correct visual analog scale scores on the AbilityQ[28]), and moderate to good arm motor control (scores of >18/66 on the Fugl-Meyer Assessment arm section[29]).After eligibility was confirmed, half of the participants were randomized to anexperimental group, and half were randomized to a sham intervention group.[26]

Observers

The two observers (both senior physical therapists) had 14 and 27 years of experience, respectively, across a wide range of diagnoses, including stroke. Before the trial, the observers were trained in obtaining the measurements using a detailed measurement protocol (the protocol, in Dutch, is available from the first author). They pretested the protocol on three participants with stroke. The observers had no pretrial experience with a hydrogoniometer and were not involved in the design of the study or the treatment of the participants.

PROM Measurement Procedure

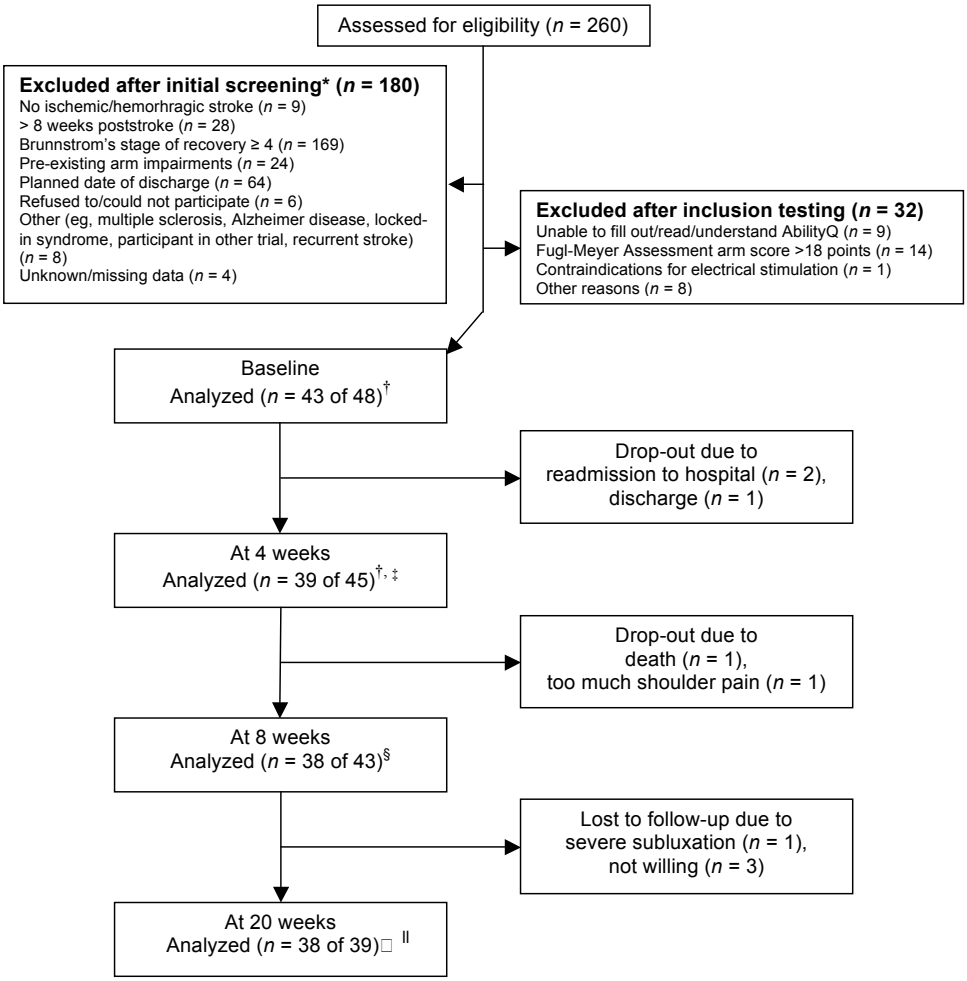
All PROM measurements were obtained with a masked fluid-filled hydrogoniometer (MIE Medical Research Ltd, Leeds, United Kingdom). The measurement

procedure was similar to the one described in detail in an earlier publication[25] but was expanded to include wrist extension assessments. Each participant was independently assessed by the two observers at baseline and after 4, 8, and 20 weeks. Each time, one observer carried out the passive movement, and the other observer read the goniometer. The observers then switched roles. They were unaware of each other's results because they used separate score sheets and were instructed not to discuss or mention the values found. The measurement sequence was as follows: shoulder external rotation, shoulder flexion, and elbow extension with the participant in the supine position and then shoulder abduction, forearm supination, and wrist extension with and without finger flexion while the participant sat on an adjustable plinth with the back supported. The observers carried out all measurements in the same fixed order.

Data Analysis

The variance components and their two-way interactions were calculated for the measurement conditions of participants (n = 48), time (four assessments over time), and observers (n = 2) by analysis of variance (type III sum of squares). Initially, the allocated intervention was also included in the calculation of variance components. However, for shoulder PROM, the variance component for intervention could not be estimated, indicating a redundancy. We therefore decided not to include intervention in the calculations of variance components. In case of missing data (eg, because of participant dropout or vacation taken by one of the observers), only data from participants who were assessed by both observers were used in the analysis. Error variance was calculated as the sum of all variances minus participant variance. The relative contributions of the sources of variation to this error variance were expressed as percentages. The agreement between the PROM ratings of the observers was calculated (see Streiner and Norman[23 [p159]] for formulas) by means of interobserver reliability coefficients and accompanying 95% confidence intervals (CIs). Because the reliability coefficient alone did not indicate the magnitude of disagreement between the observers, the standard errors of measurement (SEMs) [SDx$\sqrt{}$(1-r)] and SDDs (1.96x$\sqrt{}$2xSEM) also were calculated. First, for the disagreement between observers within a measurement occasion, we used the standard deviation of the mean difference in ratings between the observers per movement. Second, for the disagreement among all observations over time ("overall") the standard deviation of all observations per movement was used. All analyses were performed with SPSS (version 18, SPSS Inc, Chicago, Illinois).

Figure 1 Flow of participants through each stage of the trial from initial screening by physician to follow-up measurement.



* If a participant was excluded for more than one reason, then all reasons were reported separately. †Five participants were assessed by one observer only. ‡One participant missed the four-week assessment due to poor weather conditions. §Four participants were assessed by one observer only, and one participant was not assessed at eight weeks because of temporary admission to a hospital. || One participant was assessed by one observer only.

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Results

Figure 1 shows the flow of participants through each stage of the trial. The characteristics of the 48 participants are shown in Table 1. In general, they had restrictions in PROM for all seven arm movements, especially shoulder movements. They had a median score of 5.5 on the arm section of the Fugl-Meyer Assessment.

Table 1 Baseline characteristics of the 48 participants[a].

Characteristic	Values
Age (yr), mean (SD)	57.8 (11.9)
Days after stroke, mean (SD)	44 (14.0)
Sex, no. of men/women	28 / 20
Paretic side (left/right), no.of participants	21 / 27
Stroke type (ischemic/hemorrhagic), no. of participants	39 / 9
Fugl-Meyer Assessment arm section score, median (IQR)	5.5 (4-10.75)
Shoulder PROM (degrees), mean (SD)	
External rotation	31.7 (19.4)
Flexion	126.7 (30.6)
Abduction	101.7 (44.1)
Elbow/forearm PROM (degrees), mean (SD)	
Extension	2.5 (7.3)[b]
Supination	77.3 (11.6)
Wrist PROM (degrees), mean (SD)	
Extension with fingers extended	55.7 (17.0)
Extension with fingers flexed	63.1 (13.0)

[a] IQR = interquartile range, PROM = passive range of motion

[b] A value of 2.5 degrees indicates elbow flexor contracture.

Figure 2 shows the separate variance components for the results obtained from shoulder external rotation as an example. The contribution of error variance (Table 2) to total variance ranged from 31% (wrist extension with flexed fingers) to 50% (supination). The interaction of participant and time made the largest contribution to error variance, ranging from 59% (forearm supination) to 81% (elbow extension).Time made a smaller contribution to error variance, especially for shoulder movements

(17 %-24%) and forearm supination (19%). Time did not contribute to the variance in the elbow joint. The interaction between participants and observers contributed only marginally to error variance (0%-4%); the same was true for the main effect of the observers (0%-2%). Residual (unexplained) variance contributed between 7% and 17% to error variance, and this contribution was generally lowest for shoulder movements. Table 3 shows the overall interobserver reliability coefficients (and 95% CIs) and SEMs and SDDs in both single sessions ("observers") and overall for the seven arm movements.

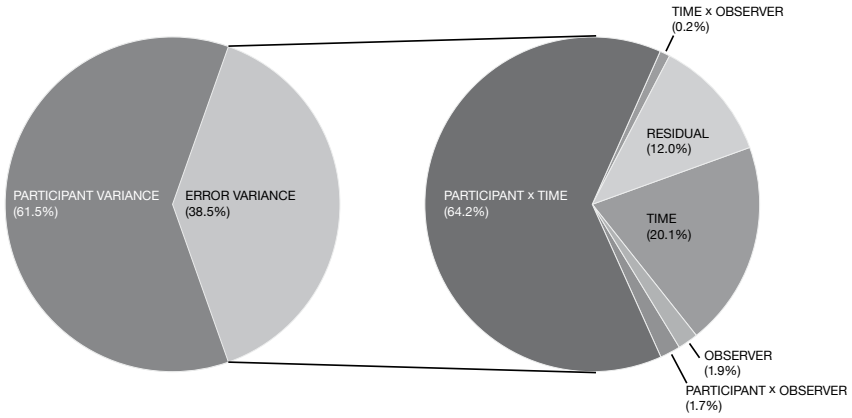

Figure 2 Variance components of shoulder external rotation. Total variance (left circle) comprised participant variance (main effect) and error variance. Several sources contributed to error variance. These sources (right circle) comprised main effects (time and observer), interaction effects (participant × time, participant × observer, and time × observer), and residual variance, all expressed as percentages of error variance.

Discussion

When different observers independently assess a joint range that does not change over time, interobserver reliability generally will be good provided that standardized protocols[17] are used and the observers are trained.[30] In addition to common sources of measurement variation, the development of contractures, hypertonia, and shoulder pain may complicate and negatively influence the reliability of PROM measurements in patients after stroke. We found that PROM assessment with a standardized protocol, a hydrogoniometer, and two trained observers yielded high interobserver reliability indexes (.89-.97) for seven arm movements. We also found that error variance made a large contribution (31%-50%) to the variation in measurement results, with the participant × time interaction being the largest source of variance. The SDDs ranged from 6 to 22 degrees and were largest for shoulder movements.

Table 2 Estimated variance components and their contributions (in percentages) to the error variance of the repeated measurements of seven arm movements (n = 48).

	Shoulder					Wrist	
Variance component	**External Rotation**	**Abduction**	**Flexion**	**Elbow Extension**	**Forearm Supination**	**Flexion With Extended Fingers**	**Flexion With Flexed Fingers**
Participant	385.0	1234.8	641.2	45.3	118.0	197.0	174.4
Error variance	241.3	702.2	377.1	34.4	117.8	115.5	77.9
Time	48.5	118.6	91.3	0.0[a]	22.3	3.2	6.5
Observer	4.5	0.3	0.7	0.0[a]	2.6	2.4	1.5
Participant × Observer	4.1	6.8	4.0	0.1	4.1	2.8	0.2
Participant × Time	154.8	524.1	244.6	27.7	69.6	88.7	59.4
Time × Observer	0.4	3.8	0.0[a]	0.6	0.8	0.4	0.0[a]
Residual variance	28.9	48.7	36.5	5.9	18.4	18.1	10.3
Total variance	626.4	1937.0	1018.4	79.7	235.8	312.5	252.3
% error variance[b]	38.5	36.3	37.0	43.1	50.0	37.0	30.9
% contribution to error variance of:							
Time	20.1	16.9	24.2	0.0	18.9	2.8	8.3
Observer	1.9	0.0	0.2	0.0	2.2	2.1	1.9
Participant × Observer	1.7	1.0	1.1	0.4	3.5	2.4	0.3
Participant × Time	64.2	74.6	64.9	80.6	59.1	76.8	76.2
Time × Observer	0.2	0.5	0.0	1.8	0.7	0.3	0.0
Residual variance	12.0	6.9	9.7	17.2	15.6	15.6	13.3

[a] Negative variance components (ranging between -0.027 and -0.517) were set to 0.
[b] Error variance expressed as a percentage of the total variance. For example, for shoulder external rotation, the calculation would be as follows: total variance (626.4) minus participant variance (385.0) equals error variance (241.3); error variance therefore represents 38.6% of total variance.

Table 3 Interobserver reliability coeficients (and 95% Confidence Intervals),Standard Errors of Measurement (SEMs), and Smallest Detectable Differences (SDDs)[a].

	Shoulder					Wrist	
Variable	**External Rotation**	**Abduction**	**Flexion**	**Elbow Extension**	**Forearm Supination**	**Extension With Extended Fingers**	**Extension With Flexed Fingers**
Overall reliability (95% confidence interval)	.94 (.91-.96)	.97 (.95-.98)	.96 (.93-.97)	.92 (.89-.95)	.89 (.84-.93)	.93 (.90-.96)	.96 (.93-.97)
SEM (observers)	2.0	1.9	1.9	1.0	2.2	1.7	1.0
SDD (observers)	5.4	5.2	5.2	2.7	6.2	4.7	2.6
SEM (overall)	5.9	7.6	6.6	2.4	4.9	4.6	3.3
SDD (overall)	16.3	21.2	18.3	6.8	13.8	12.8	9.1

[a] "(Overall)" refers to the overall reliability, SEM, and SDD for the observers over time; "observers" refers to the SDD

and SEM for a single measurement session.

Interobserver reliability.

The interobserver reliability of our two physical therapists was high in all seven arm movements. These results are in concordance with previous findings.[25,31] The reliability coefficient for shoulder abduction (.97) was higher than previously reported values (intraclass correlation coefficients = .84 to .87),[25] and forearm supination resulted in the lowest reliability coefficient (0.89). Supination intraclass correlation coefficients were higher than previously reported values (.94 to .98),[25] but the accompanying 95% CI's were wider (.84 to .98). Because all of our measurements were obtained with the same measurement protocol,[25] the values that we obtained may have resulted from the use of a larger sample. Differences in sample size may also explain the narrower 95% CIs (.89 to .95) for elbow extension measurements in the present study than in a recent study (0.68 to 0.97)[24] of 13 patients with stroke and elbow flexor spasticity. Because larger samples generally yield more precise estimates of reliability coefficients (indicated by narrower CIs and smaller SEMs), the results of the present study can be interpreted with more confidence than the results of previous results. To our knowledge, the reliability of wrist movements has not been reported in patients with stroke. We found that the assessment of wrist extension revealed slightly higher reliability coefficients and slightly lower SEMs when the fingers were flexed instead of extended. The long finger flexors typically show increased resistance to passive stretch (hypertonia), possibly partly because of the rapid development of wrist flexor contractures.[10,32] This condition occurs especially in patients with limited arm function and clearly applied to our participants. Therefore, wrist flexor hypertonia or contracture may have had a slight negative influence on the reliability of the assessments of wrist extension with extended fingers. This hypothesis is supported by the fact that residual variance (to which wrist flexor hypertonia or contracture may also have been a contributing factor) accounted for 16% of the error variance of the PROM measurements; when the fingers were flexed, the value was 13%. In conclusion, the resulting high reliability coefficients suggested that our standardized measurement protocol may be of use for other observers under comparable circumstances.

Variance components

While assessing seven arm movements on four occasions during a 20-week time period, we found that the participants in our sample were the largest source of variance. This finding indicates that the participants could be distinguished on the basis of their arm PROM; they had a large variety of arm joint ranges. Error variance explained between 31% and 50% of total variance in the PROM values. Overall, time and the participant × time interaction were responsible for more than 78% of the

variation in measurement results, with the participant × time interaction contributing the most. This interaction effect indicates that the effects of time on PROM of the arm were different in different participants, in accordance with clinical observations. In some participants, PROM increased over time probably as a result of natural neurological recovery or rehabilitation, whereas in other participants, PROM may have decreased over time as result of contracture formation. The main effects of time and observers did not contribute to the variation in the results for elbow extension PROM. For the latter, the participant × time interaction (81%) and random variance (17%) made large contributions to error variance. Clinically, this finding indicates that over time, elbow extension developed quite differently in the participants. Observers contributed only marginally to the variation in measurement results, with a maximum of 4% (forearm supination). This finding indicates that the differences between the values obtained by the two observers were small, resulting in high interobserver reliability coefficients. The fact that one observer performed the passive movement and the other positioned and read the goniometer may have led to this finding. On the basis of these results, we argue that arm PROM assessments with a hydrogoniometer in patients after stroke should be performed by two observers. Clinically and economically, assessments by two raters may not always be practical or feasible.[25] Therefore, clinical and economical arguments must be weighed against scientific arguments (reliability) in each situation. Further research is needed to analyze the influence of the number of observers on measurement results. Residual variance in the PROM measurements in our sample may be explained partly by random variations in PROM over time within a participant but may also have been caused by random variations in the force applied by the observers or the alignment of the hydrogoniometer between measurements.

Smallest Detectable Differences

Overall, the SDDs ranged from 3 degrees to 22 degrees and were largest for shoulder movements. Taking shoulder external rotation as an example, these data mean that a change of 17 degrees or more over a period of 20 weeks (overall SDD) represents a change in PROM with 95% certainty. Physical therapists and clinicians can use the overall SDD to evaluate their patients' changes in arm PROM between admission and discharge. Similarly, researchers can use them to interpret changes in participants in clinical trials. The SDDs obtained in single sessions by our two observers also may serve another purpose. Taking elbow extension as an example, our results show that a difference of more than 3 degrees between two observers in one session indicates a significant difference in their measurements with 95% certainty. In stroke research the (Modified) Tardieu Scale[33] is increasingly being used to differentiate muscle contracture from spasticity. Because this scale relies partly

on PROM measurements, the SDD can be used as a threshold value that must be exceeded to ascertain with 95% confidence that the angles between between R1 ("catch") and R2 ("end range") are significantly different and that spasticity is indeed present. Similarly, the overall SDD for elbow extension (7º) can be used to indicate significant changes in elbow PROM over longer periods of time. Comparing our SDDs with those reported in the literature[24,25] is hindered partly by the influence of sample sizes on SEMs (larger samples produce smaller SEMs) and therefore SDDs (smaller SEMs produce smaller SDDs). Because of our larger sample, our data can be used to interpret differences or changes in PROM with more confidence.

Limitations

An important limitation of the present study is that half of our participants were allocated to a combination intervention consisting of static muscle stretch and electrical stimulation. Although the results of this intervention were not significantly different from those of a sham intervention and the variance component for intervention could not be estimated, we cannot rule out the possibility that the development of the outcomes over time was confounded by the intervention and therefore that the intervention contributed to residual variance. Initially, we also tried to verify whether shoulder pain and hypertonia of shoulder internal rotators, elbow flexors, and wrist flexors were sources of error variance. However, adding these variables to the statistical analysis led to a substantial number of unstable variance components. Therefore, we chose to analyze a simpler model. The best fitting model was subsequently applied to all other arm movements by setting all negative variances to 0. Future research is needed to verify which factors are actually responsible for random variance, for example, by comparing patients with and without contractures, hypertonia, and pain. Another limitation is that, despite pretrial training, we cannot say for certain whether the competence of our two observers had any influence on the study results. We selected people with stroke and poor recovery of arm motor control. A median score of 5.5 on the Fugl-Meyer Assessment arm section at about 6 weeks after stroke means that a patient typically shows only hyperreflexia or (partial) mass synergy patterns, which are usually dominated by shoulder internal rotation and finger and elbow flexion, at best. Although our results can be generalized only to similar groups of patients, such patients represent about 36% to 52% of those with subacute stroke between two weeks and three months after stroke.[19] Finally, our results may indicate reliability within observers because it is generally recognized that intraobserver reliability is bound to be higher than interobserver reliability.[23]

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Chapter 7

General Discussion

This thesis focused on three separate, interrelated topics that play a role during the rehabilitation phase of patients after stroke. First we set out to answer the question how often hypertonia develops in the hemiplegic elbow in the first six months poststroke and whether it would be possible to predict it's development based on the degree of arm motor control. The second research question was whether static arm muscle stretching programmes would be effective in preventing the development of muscle contractures, hypothesizing that this would also positively influence (or rather reduce) the development of poststroke shoulder pain, hypertonia / spasticity and restrictions in daily basic arm activities or arm motor control. Finally, we focused on the question whether passive arm joint range of motion (PROM), an important outcome measure used to determine the degree of contracture, can be assessed reliably by physical therapists. In this concluding chapter, the main findings for these three different research topics will be summarised, the strengths and limitations of these studies will be discussed and implications for clinical practice and future research will be described.

Development of hypertonia in patients after stroke

Summary of the main results

In *Chapter 2* the results of a prospective cohort study were described in which 50 patients with a first-time ischemic stroke and an initial arm paralysis were followed for up to six months poststroke. The results showed that the incidence rate of hypertonia reached its maximum before the third month poststroke (30%). A large portion (42%) of the patients had hypertonia at three and six months. The study also revealed that participants with poor motor control, which was defined as 18 points or less on the arm section of the Fugl-Meyer Assessment (FMA), at 48 hours poststroke were 13 times more likely to develop hypertonia in the first six months poststroke than those with FMA scores more than 18 points. Additionally, the risk of developing hypertonia increased significantly over time.

Discussion

The goal of the prospective cohort study was to monitor the development of hypertonia in the flexor muscles of the hemiplegic elbow. The reason for collecting data on hypertonia development was to check the hypothesis that stroke survivors with poor recovery of motor control are more at risk of developing hypertonia than those with a better level of recovery. More importantly, detailed information about the development of hypertonia in the hemiplegic arm could serve to better underpin the need for interventions aimed at preventing the development of not only hypertonia, but also of spasticity and contractures.

Hypertonia has both a neural and a biomechanical component. Contracture is

an important contributor to hypertonia.[1,2] This is illustrated by the finding that increased passive muscle resistance was present independent of muscle activity monitored via electromyography,[3] a much used electrophysiological technique to evaluate spasticity.[4] These findings suggest that the presence of poststroke hypertonia *indirectly* hints at the presence of contracture. Admittedly, it would have been more straightforward to monitor the development of contracture *directly* by using goniometry. In fact, the passive range of elbow motion was assessed in 31 of the 50 participants, but unfortunately an important amount of data was missing. Fortunately, other authors recently *directly* assessed and monitored contracture development in the first 6 months following stroke.[5] Their results showed that 52% of the cohort (n = 165) developed at least one contracture, that contractures were most common at the shoulder and the hip and more common in those with severe strokes (> 5 points on the National Institutes of Health Stroke Scale). Similarly, our results showed that 42% of our cohort (n = 50) had developed hypertonia (MAS ≥ 1+ in the elbow flexors) and that hypertonia was more common in those with the poorest level of recovery of arm motor control (the latter probably being the patients with the most severe strokes). These similarities in findings, and the fact that contractures are an important contributor to hypertonia suggest that the development of hypertonia and contracture go hand in hand. More research is needed to determine the strength of this relationship.

Strengths and Limitations

This was the first-ever longitudinal study describing the incidence and prevalence of elbow flexor hypertonia in the first 6 months poststroke, and the predictive value of arm motor control on its development. Because hypertonia has been associated with serious poststroke impairments in body functions and activity limitations, it is of paramount importance to predict and counter its development as soon as possible. The results of this study have not only given more insight into the poststroke development of hypertonia over time, but they have also shown that the (score on the) arm section of the Fugl-Meyer Assessment (FMA) can be used to predict who is most at risk of developing hypertonia: patients who score 18 points or less on the FMA at two days poststroke have a 13 times higher risk of developing hypertonia in the subsequent six months. This knowledge can help rehabilitation clinicians and therapists to recognize patients who are at greater risk of developing hypertonia, so that effective preventive measures can be taken as soon as possible in daily clinical practice.

A limitation of this study was that only the development of elbow flexor hypertonia was monitored. Although hypertonia of elbow flexor muscles can impede functional

use of the arm (e.g. reaching with the hand, putting on a coat or sweater), hypertonia development of shoulder extensors, adductors, internal rotators and flexors of the wrist may impede arm function even more. As a consequence, the overall prevalence and incidence of hypertonia of the affected arm after stroke may have been underestimated in this study. Moreover, hypertonia is commonly assessed using the original five-point Ashworth Scale (AS)[6] or the six-point Modified Ashworth Scale (MAS).[7] For this study the MAS was used because it was found to be reliable.[7-10] More importantly, it was selected because the MAS was the tool most used by other authors, which would supposedly facilitate comparison of results. Despite this assumption, comparison with other authors proved to be difficult. Although most authors also used the MAS, they defined clinically relevant hypertonia differently by choosing different cut-off levels. In the absence of agreement about the definition of clinically relevant hypertonia, mutual comparison of results is hindered and general conclusions about incidence and prevalence of hypertonia cannot be drawn. In a sense, our choice to select yet another different cut-off score (1+ or higher) on the MAS during the cohort study did not contribute to this comparison. However, in *Chapter 2* we explained this choice by arguing that MAS levels of 1+ or higher represents a level of clinically relevant hypertonia that can also be quantified biomechanically[11] and which may be the minimal degree of hypertonia that can be associated with the development of contracture.

Implications for clinical practice and future research

Based on the excellent psychometric properties and the predictive value of the arm section of the FMA, we recommend that it be used routinely to assess arm function during poststroke rehabilitation. The advantage of the body function level FMA is that the motor tasks of this assessment tool can be performed by patients with various levels of arm motor recovery. This is not to say that the use of activity-level arm function tests is discouraged. However, many of the motor activities of such widely recommended tests (e.g. the Action Research Arm Test, Wolf Arm Function Test, Frenchay Arm Test) require a higher level of arm motor control such as the ability to reach, grasp or manipulate objects. Patients with poor motor control cannot perform such motor activities, which will repeatedly result in low scores on these tests, making potential small changes in arm motor control go unnoticed (floor effect). The FMA appears to be more sensitive to small changes, especially in those with poor arm motor recovery.

Literature regarding the assessment of hypertonia clearly shows that the presence of resistance to passive stretch after stroke is still being considered as, and confused with, spasticity. This is illustrated by the fact that the MAS is still widely

used to quantify spasticity,[eg,12] even when it has long been established that the MAS evaluates resistance to passive stretch caused by a combination of soft tissue contracture and spasticity,[13] and that it is unable to differentiate whether the cause of that resistance is neural or peripheral.[14,15] Moreover, research into the validity and reliability of the MAS has revealed inconclusive results.[eg, 10,16] A differentiation between the neural and peripheral contributions to movement resistance can be made using the seemingly more accurate Tardieu Scale,14 but it's reliability and validity has not yet been established in a population of patients after stroke.[12] There is also lack of consensus regarding a definition of clinically relevant hypertonia, which we defined as a level of resistance to passive stretch that actually represents a degree of hypertonia that necessitates (therapeutic) intervention. In *Chapter 2* we explained our choice to select MAS scores of at least 1+ as a cutoff point for clinical relevant hypertonia, but this choice needs future verification. Many of the aforementioned uncertainties probably stem from a generally limited understanding of the pathophysiology of spasticity and the various associated neurological and biomechanical features that come into play after stroke.[17] Although it is outside of the scope of this thesis, it is clear that future research is required if we are to resolve these issues.

The results of the cohort study showed that hypertonia (and therein contractures) developed in a large proportion of patients with stroke, predominantly within the first three months poststroke. The results also showed that poor arm motor control at 48 hours poststroke is a serious risk factor for the development of hypertonia. Considering the problematic secondary effects of hypertonia and contracture development, it seems to be of paramount importance to prevent these developments as soon as possible after stroke, especially in those first three months.
At the beginning of the past decade, Gracies et al. already stated: *"For optimal efficacy, therapies aimed at improving function should address both muscle shortening and muscle overactivity; measures to relax overactive muscles should be combined with physical treatment to lengthen them."*[18] The results from the cohort study suggest that this may be particularly important for those patients with the worst level of arm motor control, as they run the highest risk of developing hypertonia. The efficacy of two different interventions, aimed at lengthening overactive muscles in an attempt to prevent the development of soft tissue changes and to minimize the level of hypertonia, are discussed in the next paragraph.

Efficacy of treatments with static arm muscle stretching programmes

Summary of the main results: single-modality pilot RCT

In *Chapter 3* the results of a pilot randomised controlled trial (RCT), investigating a static arm muscle stretching programme applied as a single-modality treatment approach, are described. All 19 participants underwent conventional rehabilitation care. Nine participants additionally received a static arm muscle stretching programme for two 30-min sessions a day, five days a week, for five weeks. Comparison of the experimental with the control participants after five weeks showed that the additional stretching programme significantly slowed down development of shoulder abduction contracture. Descriptive analysis of the 10-week measurements showed further decreases of PROM in both groups. Arm motor control, as represented by the scores on the FMA arm section, was better in the experimental group at the beginning of the study, a difference that reached significance after five weeks. This trend seemed to continue after 10 weeks for the remaining participants of the experimental group, but was probably biased by baseline differences. The percentage of participants with pain at the end range of the shoulder movements remained high in both groups from baseline to 10 weeks. Especially in the first five weeks of the trial, the participants of both groups gained more independence in daily life activities as indicated by the Barthel Index. Despite some of these positive trends, no between-group differences were found in resistance to passive stretch (hypertonia), arm motor control, shoulder pain or independence in activities of daily life.

From a single-modality to a multimodal RCT

The results of the pilot trial were ambiguous. On the one hand, the efficacy of the intervention seemed to be very limited, because no between-group differences were found on most of the outcomes. On the other hand, the significant between-group difference in shoulder abduction PROM seemed to suggest that the intervention resulted in slowing down contracture development of the shoulder adductors. At the time that the results of the pilot trial were analyzed, a similar positive result was described for shoulder external rotation.[19] However, the overall conclusion, that there was no evidence that static arm stretching programmes were effective, was drawn after two meta-analyses.[20,21] Possible explanations for the lack of (statistical significant) effects were the lack of statistical power to detect any differences (small sample sizes) and an inadequate duration of stretching. These factors may also have played a role during the pilot trial. The design of the pilot trial was used as a blueprint for the next RCT, whereby two of the most probable limitations of the pilot trial were adjusted: the small sample size and the

possibly inadequate duration of the stretch.

The small number of participants (n = 19) that could be recruited during the pilot trial suggested that the selection criteria were too strict. For example, several patients were excluded for participation because they had severe neglect, loss of positioning sense or because they used medication for pain and spasticity. Furthermore, the dropout rate was high. Eventually, only 10 participants were available for the final 10-week assessment because several participants were discharged before the end of the treatment period and no effort was made to motivate them to undergo the final measurements. During the second trial, participants with neglect, severe loss of positioning sense and participants who used medication for pain or spasticity were included *(Chapter 4)*. These participants received extra skin checks and the use of medication was monitored. Also, participants with recurrent strokes were included. To minimize patient dropout due to discharge, the treatment period was shortened from 10 to eight weeks and every effort was made to motivate participants to undergo all planned measurements even after withdrawal from the allocated intervention.
Although an inadequate duration of the stretch could be the reason for lack of an effect of static stretching programmes, the intensity of stretch (i.e. the force level at which the muscle is stretched) may also have been inadequate. To increase the duration of the stretching, intervention time was increased to (an expected) limit of workability, i.e. from 60 to 90 minutes a day. One could still argue that this was insufficient, especially since the Medical Disability Society recommends to put shortened human muscles through a full stretch for two hours in every 24 hours.[22] However, applying the stretch programme for more than 90 minutes a day was already considered unworkable during an intensive clinical rehabilitation programme. On the other hand, increasing the intensity of stretch was also taken into consideration and subsequently achieved by making use of the muscle stretching capabilities of another intervention. This created a multimodal approach to the problem. The notion of combining different treatment modalities to increase intervention efficacy was in part derived from other fields of medicine, which influenced the decision to combine static arm stretch positioning with an intervention that would preferably positively influence both the neural and biomechanical components of hypertonia, hence increasing the intensity of the intervention. For this purpose, neuromuscular electrical stimulation (NMES) was selected.

Summary of the main results: multimodal randomized controlled trial
In *Chapter 4* the results of the second RCT, investigating a static arm muscle stretching programme applied in conjunction with NMES, are described. All 46

participants received conventional rehabilitation care. Half of the participants (*n* = 23) were allocated to the experimental intervention, consisting of a static arm muscle stretching programme of two 45-min sessions a day, on five days a week, for eight weeks with simultaneous motor amplitude NMES. The control participants received sham arm positioning (i.e. no stretch) and sham NMES (i.e. transcutaneous electrical nerve stimulation with no motor effect) to the forearm only, using a similar frequency and duration. Despite the interventions, both groups showed similar reductions in mean PROM across most arm joints. Shoulder pain prevalence increased from 37% at baseline to 52% after eight weeks. Overall, pain severity also increased, particularly on movement and at night. Improvements in the scores of the Leeds Adult/Arm Spasticity Impact Scale and FMA over time indicated an improved capacity to perform basic arm activities and improved arm motor control. Overall, the prevalence of elbow flexor hypertonia and spasticity jointly increased up to 55% around the eight week outcome measurement.

Despite some positive changes over time (increased motor control), no significant between-group differences were found in arm passive range of motion (contractures), shoulder pain, daily basic arm activities, hypertonia and spasticity, arm motor control and shoulder subluxation.

Discussion

The results of the two RCT's presented in this thesis cannot be discussed without dwelling on evidence that has accumulated in literature in the past decade regarding the effects of static arm muscle stretching programmes for the hemiplegic arm.

Overall, the conclusion from two meta-analyses was that static arm stretching programmes do not result in any clinical relevant advantages for the patients.[20,21] Some small significant effects on shoulder PROM in favour of the experimental groups in two of the studies suggested that the programmes could be effective in *slowing down* the development of shoulder external rotation[19] or shoulder abduction *(Chapter 3)*[23] contractures of the hemiplegic arm. However, these results were not confirmed by other studies. Pooled trial data resulted in a non-significant (p = .26) overall effect size of 1.12 with a mean difference of 2.17 degrees (95% CI: -1.63, 5.97) on joint mobility (range of motion) in favour of stretching.[21] Few clinicians and physical therapists would argue that a treatment effect this small would be clinically important. Such a small change in PROM cannot even be assessed reliably. In fact, the minimum difference (i.e. the smallest detectable difference) that needs to be exceeded to be 95% confident that, over time, a real change in passive range of motion has occurred ranges from 6 to 22 degrees for the different arm movements (*Chapter 5* and *Chapter 6)*. Regardless of the effects

on joint mobility, reviewers also failed to show any effects of stretch on pain, spasticity, and activity limitation.[21] In addition, no effects were found on resistance to passive stretch (hypertonia), arm motor control, independence in activities of daily life and shoulder subluxation (*Chapter 3* and *Chapter 4*). The interventions may even have resulted in adverse events because some participants from the experimental group showed an increase in pain,[24] medication for pain and spasticity were prescribed more frequently and protocol compliance was lower (*Chapter 4*). Although there were no significant between-group differences in pain, these findings may indicate that the experimental programme was not well tolerated by some participants. Such concerns have been raised previously.[25]

Strengths and Limitations

Work on the two RCT's presented in this thesis has spanned a period of almost 10 years. This rather long time-frame was considered an advantage since it made it possible to adjust the design and the statistical analyses of the multimodal trial both according to the results of the pilot trial as well as findings in literature published between 2003 and 2007. For example, the multimodal trial was designed in a period in which it became clear that a single-modality static arm stretching programme had very little clinical impact. As a result, a multimodal approach for the larger RCT was chosen. Both RCT's were designed according to the recommendations of the CONSORT Statement.[26] Thus, both RCT's were robust in design. This is illustrated by the fact that the publication of the pilot trial (*Chapter 3*) has been rated with a methodological quality score of 7/10 on the PEDro-scale.[27] The experiences gained during the pilot trial enabled us to design an even more robust second RCT.

The research presented in *Chapter 3* and *Chapter 4* has contributed to the confirmation that restrictions in range of motion of the hemiplegic shoulder and wrist can develop quite rapidly in patients with poor arm motor control.[23,25,28,29] Our findings also lend support to the notion that, although TENS is commonly used to treat shoulder pain after stroke, there is little evidence that (in general) it is clinically effective in providing pain relief.[30,31] We used TENS in our control group, but as we found no significant pain reduction both within and between the two groups, we are confident that we managed to select a proper sham treatment that did not confound the main results regarding shoulder pain. Our overall conclusions are also in concordance with previous results, confirming that static arm muscle stretching programmes cannot prevent a decrease in arm joint PROM resulting from contracture formation. This knowledge can be used in search of other, more effective interventions aimed at contracture prevention.

The limitations specific to each of the two RCT's have been discussed as part of *Chapter 3* and *Chapter 4*. An important general limitation of the SEPP-trial was that an intention-to-treat analysis, the preferred analysis for an RCT, could not be performed. A full application of the intention-to-treat approach is possible only when complete outcome data are available for all randomised participants.[32] During the pilot trial, the sample sizes per group were limited, and not enough care was taken to follow up those patients who withdrew from the allocated treatments. This inevitably resulted in missing data, rendering a full intention-to-treat analysis impossible. Therefore, the clinical effectiveness of the intervention may have been overestimated. This specific limitation was resolved during the PAESIS-trial. Another general limitation was that the research question, i.e. whether sufficient muscle length would indirectly reduce the main body functions such as hypertonia, spasticity and shoulder pain, could not be answered because muscle length was not influenced by the interventions. One could argue that the lack of change in muscle length corresponded to a lack of change in hypertonia, spasticity and shoulder pain, but a causal relationship could not be demonstrated.

Implications for clinical practice and future research.

Knowledge gained during the writing of this thesis has learned that single-modality static arm muscle stretching programmes do not produce clinically important changes in joint mobility, shoulder pain, resistance to passive stretch (hypertonia), spasticity, arm motor control, activity limitations and independence in ADL in people with stroke. Even a higher-intensity multimodal approach (*Chapter 4*) did not result in positive effects for the patients, thereby also confirming the results of a recent randomized trial in which a similar multimodal approach was chosen to prevent the development of wrist contractures.[33] Some findings even suggest that for some participants the static arm muscle stretching programmes are not well tolerated. As such, the conclusion seems justified that static arm muscle stretching programmes as described in the literature should no longer be performed in the subacute phase following stroke. As a consequence, the stroke rehabilitation team is left with an increasingly difficult challenge to prevent the development contractures, hypertonia and spasticity and its associated secondary problems such as shoulder pain and restrictions in performance of daily life activities in a considerable number of patients after stroke who have poor motor control.

From a research perspective, it would be worthwhile to explore what renders the current static arm muscle stretching programmes ineffective. The finding, that this type of intervention does not work, raises some interesting questions.

First of all it challenges the commonly accepted hypothesis that sustained stretch can improve muscle length in patients with neurological conditions in general and in patients after stroke in particular. Although periods of sustained stretch resulted in prevention of sarcomere loss and maintenance of normal passive range of motion in animal muscles,[34] connective tissue of patients after stroke does not seem to respond similarly to sustained stretch. It also challenges the hypothesis of (partial) restoration of reciprocal inhibition that has been proposed as one of the possible mechanisms for spasticity reduction poststroke.[35,36] Especially poststroke patients with severe motor deficits have a higher risk of developing increased resistance to passive muscle stretch (hypertonia) of the muscles responsible for an antigravity posture.[5,37,38] The acting force of hypertonia may have neutralized the acting force of the sustained stretch, and the electrical stimulation may not have effectively elicited reciprocal inhibition. Future research could e.g. be aimed at controlling the increased resistance to passive stretch during stretching or exploring whether reciprocal inhibition is actually restored in the subacute phase after stroke.

Secondly, it raises the question whether an earlier start of a preventive arm muscle stretching programme will determine the failure or success of such an approach. It has been shown that there is an inverse relationship between time since onset of stroke and the degree of passive shoulder external rotation on the paretic side (*Chapter 5*). Results from our cohort study (*Chapter 2*) also showed that hypertonia is already present in 20% of poststroke patients at 10-12 days poststroke. These and other results from literature suggest that biomechanical changes develop very rapidly in the hemiplegic arm, and that the interventions aimed at preventing these developments should be commenced as soon as possible after stroke,[19] and preferably before spasticity starts to emerge. As it is possible to predict who is most at risk of developing biomechanical adaptations (hypertonia, contracture) as early as 48 hours poststroke using the FMA (*Chapter 2*), this could also be the appropriate starting point for these interventions.

Another explanation for the failure to show an effect of the interventions could be the confounding effect of the presence of shoulder pain in some of the participants. Although the static arm muscle stretching programme showed no overall benefits for the participants, some clearly developed less, and some developed more pain during the experiment. The data of the participants that developed more pain suggests that they did not tolerate the intervention well (*Chapter 3*). This adverse effect, as noted in both study groups, was not statistically different between the groups and there were also participants who did not develop pain and tolerated the programme without complications. A sensitivity analysis based on baseline shoulder pain might have given insight into the hypothesis that patients without initial shoulder pain would positively respond to this type of intervention. However,

such a sensitivity analysis was not deemed useful because of the resulting small sample sizes per group. It could be useful to investigate whether (initial) shoulder pain confounds the effects of static stretching. Finally, further research should also be performed to investigate whether other (combinations of) interventions can be effective. For example, it may be worth investigating whether NMES of the muscles prone to shortening[39] can be effective. It may also be worth to investigate the combination of static arm stretching with the simultaneous application of heat or transcranial magnetic stimulation (TMS). Both heat and TMS are 'passive' interventions that can be used to treat patients who lack active arm motor control. Recent research has shown that heat can be an effective adjunct to developmental and therapeutic stretching techniques[40,41] and that TMS may create a homeostatic change in the brain which contributes to the normalization of muscle tone and induce arm movement.[42] Lastly, to save valuable treatment time, a triple combination of interventions can be considered. This is a common approach in medicine research and has resulted in positive results e.g. in the treatment of hypertension.[43]

One of the key goals of the static arm muscle stretching programme was to prevent the development of shoulder and arm contractures. To quantify this outcome, the PROM of several arm movements was assessed on several occasions using a (hydro)goniometer. Although overall the intervention did not produce any clinical relevant advantages for the patients, some results suggested that contracture development could be slowed down. For example, after eight weeks of positioning, the experimental participants of the multimodal trial had a statistically significant larger shoulder external rotation PROM of 13 degrees (95%CI 1-24) compared to the control participants (*Chapter 4*). It is of note that this specific result was based on a single t-test at eight weeks, and not on the original multilevel regression analysis. Despite that, it would still be interesting to ascertain whether a between-group difference of this magnitude would represent a *clinically relevant* difference in PROM. Additionally, for the interpretation of the study results of the two RCT's, it was vital that the (hydro)goniometer was able to precisely and accurately assess changes in PROM. Previous studies have shown that goniometry is prone to error, and reliability both changes from joint to joint and depends on multiple factors. As a consequence, each time PROM results are presented, the question remains as to whether these measurements are reliable, are influenced by different sources of variation and whether changes in PROM found represent clinically important changes. In the next and final paragraph this issue will be discussed.

Assessment of the reliability of goniometric passive range of motion measurements of the hemiplegic arm

Summary of the main results

The results of the two separate reliability studies, during which five (*Chapter 5*) and seven (*Chapter 6*) arm movements were assessed on three and four different occasions, respectively, showed that the assessment of PROM yielded high levels of agreement between the observers with intraclass correlation coefficients (ICC's) ranging between 0.84 and 0.99. Smallest detectable differences (SDD's) were largest for the shoulder movements. Correlations revealed that restricted range of arm motions relate to the time poststroke and coincide with pain, but concurrent validity with the Ashworth Scale, Fugl-Meyer Assessment and Barthel Index scores was limited (*Chapter 5*). The PROM measurements were influenced by error variance ranging from 31% to 50%. The participant × time interaction made the largest contribution to error variance, ranging from 59% to 81% (*Chapter 6*).

Discussion

At the beginning of this century, little was known about PROM measurements in the hemiplegic arm: literature regarding the reliability of goniometric measurements was scarce, information about smallest detectable differences (SDD) was lacking, factors associated with range of motion measurements (such as hypertonia and shoulder pain) as indicators of their concurrent validity were unknown and research into factors that might potentially influence hemiplegic arm PROM measurements had never been performed. The research presented in *Chapter 5* and *Chapter 6* of this thesis has contributed to filling these gaps in knowledge. First we established that PROM measurements with a hydrogoniometer can be performed reliably by two different raters (*Chapter 5*).[44] This finding was confirmed using a larger sample (*Chapter 6*),[45] and this time the results also indicated that the differences between the raters' values were so small that they only contributed marginally to the variation in measurement results. Although other authors already showed that shoulder external rotation[46] and elbow extension[47] PROM could be assessed reliably, the added value of our studies is that the same has been shown to be true for shoulder abduction and flexion, forearm pronation, wrist extension and wrist flexion with extended and flexed fingers. Second, our work has yielded data that clinicians, therapists and researchers can use to judge whether the changes in arm PROM of their poststroke patients or participants represent real changes in PROM with 95% certainty. For example, when a therapists aims to improve shoulder abduction PROM during rehabilitation and uses a hydrogoniometer to assess these changes, he or she can now know that changes between 0 and 21 degrees over 20 weeks of time may well be the result of random measurement errors and not even represent

a reliable change in PROM. The SDD's can also serve researchers of intervention trials in predetermining the clinically relevant difference in PROM: they must make sure that it exceeds the SDD for that particular arm movement if they want to be 95% sure that the change does not reflect the measurement error.

Strengths and limitations

Comparison of our results with the limited information in literature is partly hindered by the differences in sample sizes. Small sample sizes will yield an imprecise estimate of the reliability coefficients which is indicated by an excessively wide confidence interval.[48] Although the sample was limited to a maximum of 18 participants during the first reliability study (*Chapter 5*), results from the second study with 48 participants (*Chapter 6*) were in line with the first and previously published findings. The results from the second study also showed that the observers only contributed marginally to the variation in measurement results (maximum of 4%), indicating that the differences between the values of the two observers were small, and resulting in high inter-observer reliability coefficients. The fact that one observer performed the passive movement while the other positioned and read the goniometer may have led to these excellent results. Because we used larger sample sizes than in previous work, our results can be interpreted with more confidence.

Some limitations of the reliability studies have been discussed as part of *Chapter 5* and *Chapter 6*, but some minor limitations remain. Several patients dropped out during the pilot trial, resulting in only 12 participants with full datasets for one proper analysis of variance. To compensate for the loss of participant data over the course of the trial, the decision was made to calculate the ICC's for three different datasets that represented the three different evaluation moments of the main trial. This approach introduced dependency in the data, and the analysis of different sample sizes resulted in varying standard errors of measurement, a less precise estimate of the reliability coefficients and wider confidence intervals. The issue of patient dropout was more or less resolved during the second study, resulting in a more robust analysis. Also, in the first study[44] the SDD's were interpreted as 'overall', whereas they should have been interpreted as 'observer' SDD's as during the second study.

Implications for clinical practice and future research.

Overall, the good results of the two reliability studies during the RCT's suggest that our standardized measurement protocol may be of use for other observers under comparable circumstances, either during research projects or in daily clinical practice. This does imply that two assessors should be used during arm PROM measurements.

This may not always be practical and feasible in clinical practice because it may involve higher costs. It is therefore suggested to perform a study that investigates the reliability of arm PROM measurements comparing one rater versus two raters working together. In view of this, it may be worthwhile to assess the reliability of, for example, smartphone-based goniometric measurements in patients after stroke, provided that the goniometer can be strapped onto the patient's limb(s) so that the rater can focus on passively moving the arm without having to worry about aligning the goniometer and reading the measurement all simultaneously. Such devices could potentially limit sources of variation to the measurement results (e.g. alignment errors, reading errors) and hence improve the reliability of the measurements. Until research using one rater has been performed we argue that, at least during research, arm PROM assessments with a hydrogoniometer in patients after stroke should be performed by two trained observers. Finally, future research could also be aimed at investigating whether factors such as the number and competence of the observers, as well as hypertonia and shoulder pain are sources of variation that contribute to the measurement results.

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Summary

Summary

A considerable number of people who have suffered a cerebrovascular accident (CVA) or stroke lose the ability to use their involved arm for functional activities. The lack of recovery and the subsequent immobilisation make the arm prone to the development of complications secondary to stroke such as hypertonia, muscle contractures and shoulder pain. These impairments in body functions threaten the long-term handling and assistive use of the affected arm.

Chapter 2 of this thesis describes an investigation into the incidence and prevalence of hypertonia poststroke, and the predictability of the degree of arm motor control on its development. In *Chapter 3* the efficacy of a single-modality static arm muscle stretching programme is explored. This intervention aimed to prevent the development of hypertonia, contractures and other secondary complications in the poorly recovered hemiplegic arm. In *Chapter 4* the results of a multimodal intervention, consisting of a static arm muscle stretching programme combined with neuromuscular electrical stimulation, are presented. An important outcome measure in both these randomised controlled trials was the degree of change in passive range of motion (PROM) of selected arm joints. Information about observer reliability, smallest detectable differences and factors that are associated with, or influence the PROM measurements, are the focus of *Chapter 5* and *Chapter 6*. The general discussion in *Chapter 7* summarises the individual studies and their results, and addresses the strengths, limitations and implications for future research and clinical practice.

The introductory chapter of this thesis describes some of the most common impairments in body functions a patient can develop after stroke. Often, the negative and positive motor signs of the upper motor neurone syndrome render the hemiplegic arm inactive and immobilised, and impede voluntary motor actions. Two significant consequences of these motor signs are that the muscles have a tendency to remain in a shortened position for prolonged periods of time, and that attempted voluntary movements are restricted. Prolonged periods of both muscle spasticity and immobilisation can result in the development of arm muscle contractures. Contractures result in stiffer muscles and are associated with the development of hemiplegic shoulder pain. The combination of spasticity and contractures leads to increased resistance to passive stretch, also known as hypertonia.

In *Chapter 2*, a prospective cohort study is described in which 50 patients with a first-time ischemic stroke and an initial arm paralysis were followed for six months.

The results showed that the incidence rate of hypertonia of the elbow flexors reached its maximum before the third month (30%). A large portion (42%) of the patients presented hypertonia at three and six months. The study further showed that participants with poor motor control (with a maximum of 18 points on the arm section of the Fugl-Meyer Assessment) at 48 hours poststroke, were 13 times more likely to develop hypertonia in the first six months than those with moderate to good arm motor control (more than 18 points). Additionally, the risk of developing hypertonia increased significantly over time.

Because contracture is considered to be an important contributor to hypertonia, and hypertonia has been associated with serious poststroke impairments in body functions and activity limitations, it is deemed of paramount importance to predict and counter its development as soon as possible. Literature also suggests that there are bidirectional relationships between hypertonia/spasticity, contracture and hemiplegic shoulder pain. As such, interventions aimed at the prevention of muscle contracture development may in turn result in the prevention of the development of hypertonia/spasticity and shoulder pain.

In *Chapter 3*, a pilot randomised controlled trial (n = 19) is described in which the efficacy of a single-modality intervention, aimed at preventing arm muscle contracture development, was investigated. The results showed that the PROM of five arm movements decreased over time. Nine participants of the experimental group received an additional arm muscle stretching programme of 60 minutes per working day for five weeks. There was some evidence that the intervention significantly slowed down the development of shoulder abduction contracture (p = .042, -5.3 degrees versus -23 degrees). However, the study was underpowered, and no effects were found in resistance to passive stretch (hypertonia), arm motor control, shoulder pain or independence in activities of daily life. Upon publication of these results, other literature confirmed that single-modality static arm stretching programmes do not result in any clinical relevant advantages for patients. Possible explanations for the lack of effect were the inadequate duration and intensity of the stretch.

In *Chapter 4*, a randomised controlled trial is described in which the efficacy of a higher-intensity multimodal intervention for arm contracture development was investigated. The results of this larger trial (n = 48) showed that performing a static arm muscle stretching programme for 90 minutes per working day combined with simultaneous administration of an electrically induced stretching exercise (using neuromuscular electrical stimulation), did not result in an increase in PROM.

Despite some positive, but clinically non-relevant changes over time (increased motor control), there were also no effects on shoulder pain, daily basic arm activities, hypertonia and spasticity, arm motor control and shoulder subluxation.

The results of the two randomized controlled trials described in this thesis confirm the conclusions of other authors, and suggest that it is not possible to control or overcome (the emergence of) contractures and hypertonia in patients with poor arm motor control after stroke by using the current static arm muscle stretching programmes. Therefore, such programmes should no longer be performed in the subacute phase following stroke. Consequently, the rehabilitation team is left with an increasingly difficult challenge to prevent the development of contractures, hypertonia/spasticity and its associated secondary complications in a considerable number of patients after stroke.

One of the key goals of the static arm muscle stretching programmes was to prevent the development of shoulder and arm contractures, as reflected by a decrease in PROM. To quantify this outcome, the PROM of several arm movements was assessed on multiple occasions using a (hydro)goniometer. In *Chapter 5* and *Chapter 6*, the questions are answered whether our PROM measurements were reliable and influenced by different sources of variation as well as what magnitude of change in PROM represent clinically important changes. The overall results showed that the assessment of PROM yielded high levels of agreement between the observers, with intraclass correlation coefficients ranging between 0.84 and 0.99. These results suggest that our standardised measurement protocol may be of use for other observers under comparable circumstances, provided that two trained observers are used. Correlations have revealed that restricted range of arm motions are associated with the time poststroke and coincide with pain, but concurrent validity with assessments of hypertonia (Ashworth Scale), arm motor control (Fugl-Meyer Assessment), and performance of activities of daily life (Barthel Index) have shown to be limited. The PROM measurements were influenced by error variance, ranging from 31% to 50%. Participant × time interaction made the largest contribution to error variance, ranging from 59% to 81%. The observers contributed only marginally to the variation in measurement results (maximum of 4%), resulting in high interobserver reliability coefficients. The results regarding the smallest detectable differences presented in these two chapters can be used by clinicians, therapists and researchers to judge whether the changes in arm PROM of their poststroke patients or participants represent real changes in PROM with 95% certainty.

Chapter 7 critically reflects on the results, strengths, and limitations of the studies that are presented in this thesis. Implications for clinical practice and future research are also described. In summary, it seems clear that hypertonia develops in a considerable number of patients poststroke, and that its risk of development can be predicted at 48 hours poststroke using the score on the arm section of the Fugl-Meyer Assessment. However, final conclusions about the negative impact of hypertonia in this patient group can only be drawn when the development of hypertonia in more muscle groups (and not just elbow flexors) is monitored, and when there is a clear consensus about the definition of clinically relevant hypertonia. It seems to be of paramount importance to prevent the development of hypertonia and contractures as soon as possible poststroke, especially for those patients with the poorest level of arm motor control. An investigation into the efficacy of two 'passive' interventions, that were aimed at lengthening overactive muscles and preventing the development of soft tissue changes, has not resulted in any clinical relevant advantages for the patients. Explanations for the lack of efficacy were the relatively late start or insufficient intensity of the interventions. The results challenge the hypotheses that sustained stretch can improve muscle length, and that reciprocal inhibition is restored in patients after stroke. Finally, the reliability of the PROM-measurements that were performed during the two RCT's were shown to be good. The standardised measurement protocol that was used may be of use for other observers under comparable circumstances, although PROM assessments by two observers may not always be practical and feasible. Future research using one observer during PROM measurements may therefore be worthwhile.

Samenvatting

Samenvatting

Een groot aantal patiënten dat een beroerte (cerebrovasculair accident, CVA) heeft doorgemaakt, verliest de mogelijkheid om hun aangedane, verlamde arm in te schakelen voor functionele activiteiten. Door het gebrek aan motorisch functieherstel blijft de arm het grootste deel van de tijd geïmmobiliseerd. Als gevolg hiervan kunnen zich CVA-specifieke secundaire functiestoornissen ontwikkelen zoals hypertonie, spierverkortingen (contracturen) en schouderpijn. Deze functiestoornissen beïnvloeden motorisch herstel in negatieve zin.

In *Hoofdstuk 2* van dit proefschrift wordt een onderzoek beschreven naar de incidentie en prevalentie van hypertonie bij patiënten na een eerste CVA. Daarnaast is onderzocht in hoeverre deze negatieve ontwikkeling is te voorspellen op basis van de mate van ontwikkeling van de armmotoriek. In *Hoofdstuk 3* is de effectiviteit van een contractuur-preventieve rekhouding beschreven voor CVA-patiënten die een slecht motorisch herstel van de armfunctie hebben. Deze interventie heeft als doel om de ontwikkeling van hypertonie, contracturen en bijkomende secundaire functiestoornissen in de revalidatiefase na het CVA te voorkomen. In *Hoofdstuk 4* worden de effecten beschreven van onderzoek naar de effecten van een preventieve rekhouding in combinatie met neuromusculaire elektrostimulatie. Eén van de belangrijkste uitkomstmaten die tijdens deze gerandomiseerde effectstudies werd gebruikt was de passieve bewegingsuitslag (passieve *range of motion*, PROM) van de aangedane armgewrichten. De betrouwbaarheid van deze PROM-metingen, alsmede factoren die van invloed waren op de betrouwbaarheid, zijn de belangrijkste onderwerpen van *Hoofdstuk 5* en *Hoofdstuk 6*. *Hoofdstuk 7* vormt tenslotte de algemene discussie van dit proefschrift. Hierin wordt gereflecteerd op de bevindingen uit de verschillende voorgaande hoofdstukken.

In het eerste hoofdstuk van dit proefschrift worden enkele van de meest voorkomende functiestoornissen of symptomen beschreven die een patiënt na het doormaken van een beroerte kan ontwikkelen. De zogenoemde ‘negatieve’ en ‘positieve’ symptomen die tot uiting komen na hersenletsel zijn er vaak de oorzaak van dat bepaalde spieren spastisch worden, dat de hemiplegische arm niet of niet goed kan bewegen en dat de spieren van de verlamde arm langduring in een verkorte positie worden gehouden. Wanneer een halfzijdig verlamde arm langdurig geïmmobiliseerd blijft zullen zich op den duur contracturen ontwikkelen. Contracturen veroorzaken stijfheid in spieren en lijken gerelateerd te zijn aan de ontwikkeling van schouderpijn. De combinatie van spasticiteit en contracturen leidt tot een verhoogde weerstand bij passief bewegen van spieren. Dit fenomeen wordt hypertonie genoemd.

Hoofdstuk 2 geeft de resultaten van een prospectief cohort onderzoek weer. Tijdens dit onderzoek werden 50 acute CVA-patiënten, die bij opname in het ziekenhuis een afunctionele arm hadden, tot zes maanden na hun beroerte gevolgd. De incidentie van hypertonie in de buigspieren (flexoren) van de elleboog bereikte het maximum (30%) op drie maanden na het CVA. Op drie en zes maanden na het CVA bedroeg de prevalentie 42%. De studie heeft tevens aangetoond dat patiënten met een slecht herstel van de armfunctie (d.w.z. met een maximum van 18 punten op de Fugl-Meyer Assessment armscore, FMA) op 48 uur na het CVA een 13 keer hogere kans hadden op het ontwikkelen van hypertonie dan patiënten met een redelijk tot goede armfunctie (d.w.z. meer dan 18 punten op de FMA). Bovendien nam de kans op het ontwikkelen van hypertonie toe naarmate de tijd vorderde.

Spieren die verkorten worden ook stijver. De stijfheid van deze verkorte spieren draagt in belangrijke mate bij aan de algehele verhoogde weerstand bij het bewegen van spieren en gewrichten. Omdat hypertonie negatief samenhangt met verscheidene functiestoornissen en beperkingen in activiteiten van de arm, wordt aangegeven dat het zeer belangrijk is om deze ontwikkeling zo spoedig mogelijk na het ontstaan van een CVA te voorspellen en tegen te gaan. De wetenschappelijke literatuur op dit gebied suggereert tevens dat hypertonie/spasticiteit, contracturen en schouderpijn onderling samenhangen. Vanuit die hypothese zou het mogelijk moeten zijn om de ontwikkeling van hypertonie/spasticiteit en schouderpijn te voorkomen door primair het ontstaan van contracturen te voorkomen.

Hoofdstuk 3 beschrijft een gerandomiseerde pilotstudie (n = 19) waarin de effectiviteit van het toepassen van een contractuur-preventieve rekhouding voor CVA-patiënten is onderzocht. De resultaten hebben o.a. aangetoond dat de PROM van vijf verschillende armbewegingen in vijf weken tijd langzaam verslechterden. Om dit tegen te gaan voerden negen CVA-patiënten, naast de reguliere revalidatiebehandeling, vijf weken lang dagelijks 60 minuten de rekhouding uit. Er werden aanwijzingen gevonden dat het uitvoeren van deze preventieve behandeling de achteruitgang van de mogelijkheid om de arm zijwaarts te heffen (passieve abductie van de schouder) afremde (p = .042, -5.3 graden versus -23 graden). De onderzoekspopulatie was echter slechts van bescheiden omvang en er werden geen verschillen tussen de groepen gevonden op het gebied van hypertonie, de willekeurige motoriek van de arm, schouderpijn en onafhankelijkheid in activiteiten van het dagelijkse leven. Ten tijde van de publicatie van deze resultaten werden deze bevindingen bevestigd door verschillende andere onderzoekers. Hieruit werd de conclusie getrokken dat deze enkelvoudige vorm van contractuurpreventie geen klinische meerwaarde

had voor de patiënten. Redenen voor het gebrek aan effectiviteit zouden kunnen zijn gelegen in een onvoldoende duur en intensiteit van de rek op de arm- en schouderspieren. Dit vormde de aanleiding voor het doen van vervolgonderzoek.

In *Hoofdstuk 4* wordt een gerandomiseerde effectstudie beschreven waarin voor een langere duur en een hogere intensiteit van de rekhouding werd gekozen. Tijdens dit onderzoek voerden 23 CVA-patiënten, naast de reguliere revalidatiebehandeling, acht weken lang dagelijks 90 minuten de rekhouding uit in combinatie met het toepassen van gelijktijdige neuromusculaire elektrostimulatie. De 23 patiënten uit de controlegroep kregen een nepbehandeling (placebo) van gelijke duur. Ondanks enkele positieve veranderingen over de tijd werden er na acht weken geen verschillen tussen beide groepen gevonden in de PROM, schouderpijn, armfunctie, hypertonie en spasticiteit, de ontwikkeling van willekeurige motoriek van de arm en subluxatie van de schouder.

De resultaten van de twee RCT's die zijn beschreven in dit proefschrift komen overeen met de resultaten van vergelijkbare studies die worden beschreven in de literatuur. Hieruit kan de conclusie worden getrokken dat het, met de contractuurpreventieve rekhoudingen in de huidige vorm, niet mogelijk is om de ontwikkeling van contracturen en hypertonie tegen te gaan of te verminderen. Daarom lijkt het logisch om het gebruik van deze behandelvorm niet (meer) aan te bevelen in de (subacute) revalidatiefase fase na een CVA. De consequentie hiervan is dat het team van hulpverleners rond de CVA patiënt geconfronteerd blijft worden met de uitdaging om de ontwikkeling van contracturen, hypertonie/spasticiteit en daaraan gerelateerde functiestoornissen en beperkingen in activiteiten tegen te gaan.

Een belangrijk doel tijdens de studies naar de effecten van de experimentele rekhoudingen was om de afname van de PROM van de armgewrichten tegen te gaan. Om deze variabele te kwantificeren werden de passieve armbewegingen door twee fysiotherapeuten gemeten met behulp van een (hydro)goniometer. In *Hoofdstuk 5* en *Hoofdstuk 6* zijn de vragen beantwoord in hoeverre de PROM-metingen van deze fysiotherapeuten betrouwbaar waren en in hoeverre deze metingen werden beïnvloed door verschillende bronnen van variatie. De resultaten hebben laten zien dat de twee fysiotherapeuten hun metingen zeer betrouwbaar hebben uitgevoerd (intraclass correlatie coëfficiënten tussen de 0.84 en 0.99). Hiermee is duidelijk geworden dat het gehanteerde gestandaardiseerde meetprotocol ook geschikt is voor gebruik door andere therapeuten onder vergelijkbare omstandigheden, met dien verstande dat er twee beoordelaars worden gebruikt. De PROM metingen werden wel beïnvloed door error variatie, welke varieerde

van 31% tot 50%. De interactie tussen patiënt en tijd (variërend van 59% tot 81%) droeg voor een groot deel bij aan deze error variatie. De beoordelaars zelf droegen slecht in zeer geringe mate (4%) bij aan de variatie in meetresultaten (4%), hetgeen resulteerde in de hoge betrouwbaarheidscoëfficiënten. De gevonden waarden van de *smallest detectable differences* die in deze twee hoofdstukken zijn gepresenteerd bieden clinici, therapeuten en onderzoekers de mogelijkheid om met 95% zekerheid te kunnen bepalen hoe groot veranderingen in de beweeglijkheid van de arm- en schoudergewrichten minimaal moeten zijn om er zeker van te zijn dat deze ook daadwerkelijk een significante verandering representeren. Tot slot is aangetoond dat er een relatie bestaat tussen de afname van de PROM en de tijd die is verstreken na het CVA, alsmede het optreden van pijn. De concurrente validiteit met de metingen van hypertonie (de Ashworth Schaal), willekeurige motoriek van de arm (Fugl-Meyer Assessment) en de uitvoer van activiteiten in het dagelijkse leven (Barthel Index) bleken echter zeer beperkt.

In *Hoofdstuk 7* wordt kritisch gereflecteerd op de resultaten en de sterke en zwakke punten van de verschillende studies. Tevens wordt stilgestaan bij de implicaties die de resultaten van deze studies hebben voor de dagelijkse praktijk. Tot slot worden enkele aanbevelingen gedaan voor toekomstig onderzoek. Samenvattend kan geconcludeerd worden dat hypertonie zich ontwikkelt in een aanzienlijke groep van CVA-patiënten en dat deze ontwikkeling al op 48 uur na het CVA voorspeld kan worden op basis van de score op Fugl-Meyer Assessment. De negatieve impact die de ontwikkeling van hypertonie op CVA-patiënten heeft kan echter nog veel accurater worden beoordeeld als deze gelijktijdig in meerdere spiergroepen (en niet alleen in de flexoren van de elleboog) wordt gemonitord en wanneer er consensus wordt bereikt over de definitie van klinisch relevante hypertonie. Voorts is stilgestaan bij de redenen waarom het belangrijk is om bij CVA-patiënten, die een slecht herstel van de armfunctie vertonen, de ontwikkeling van contracturen en hypertonie zo spoedig mogelijk na het CVA te voorkomen. Deze negatieve ontwikkeling is getracht te voorkomen middels twee experimentele interventies. De interventies bestonden uit het 60 minuten per dag rekken van arm- en schouderspieren die neigen tot verkorten, of 90 minuten per dag rekken in combinatie met neuromusculaire elektrostimulatie van enkele tegenoverliggende spieren (antagonisten). Helaas hebben deze interventies niet geleid tot klinisch bruikbare resultaten. Verklaringen die kunnen worden gegeven voor het gebrek aan effect zijn de relatief late start van de interventie en een onvoldoende intensiviteit van de interventies. De resultaten van deze studies betwisten de gangbare hypotheses dat klinisch relevante contracturen tegengegaan dan wel verminderd kunnen worden met statische (duur)rek en dat het mechanisme van reciproke

inhibitie na een CVA kan herstellen. Tot slot bleek de betrouwbaarheid van de PROM-metingen tijdens de interventiestudies zeer goed te zijn. Het daarbij gehanteerde meetprotocol kan van nut zijn voor andere beoordelaars onder vergelijkbare omstandigheden. Het is wel de vraag of het gebruik van twee meettherapeuten efficiënt is. Vervolgonderzoek zal moeten uitwijzen of het gebruik van één beoordelaar tot vergelijkbare dan wel betere resultaten zal leiden.

About the author | Over de auteur

About the author

Lex Diederick de Jong was born on December the 25th, 1971 in Dokkum, The Netherlands. He completed his pre-university A-levels in 1991. In 1995 he received his bachelor's degree in physiotherapy from the Hanze University of Applied Sciences in Goningen. After his graduation he gained his first working experience as a physiotherapist during several temporary positions in nursing homes (The Netherlands), hospitals (United Kingdom) and private practices (Germany). In 1998 he found his first steady job in rehabilitation center De Vogellanden in Zwolle. Here he specialised in neurological physiotherapy in general and stroke rehabilitation in particular. Besides his clinical work he designed, organised and managed his first multicenter randomised controlled trial (RCT) whilst studying for his master's degree at the KU Leuven (Belgium). Here he earned his MSc-degree *magna cum laude* in 2004. After having written and published three publications about his first RCT in his spare time, as from 2008 he combined his clinical work with a part-time PhD-position at the Department of Rehabilitation Medicine at the University Medical Center Groningen. During this time he managed his second multicenter RCT, was member of the team that updated the clinical practice guidelines for physiotherapy in patients with stroke (for the Royal Dutch Society of Physiotherapy), and wrote and published three additional papers in completion of his PhD-thesis. In 2011, Lex started working as a lecturer at the School of Physiotherapy of the Hanze University of Apllied Sciences in Groningen.

Over de auteur

Lex Diederick de Jong werd geboren op 25 december 1971 te Dokkum. In 1989 behaalde hij aan de toenmalige Scholengemeenschap 'Oostergo' te Dokkum zijn HAVO-diploma, gevolgd door zijn VWO-diploma in 1991. De daaropvolgende vier jaren studeerde hij aan de opleiding Fysiotherapie van de Hanzehogeschool Groningen. Hier behaalde hij in 1995 zijn *bachelor's degree*. Om zijn onderzoeksvaardigheden verder te ontwikkelen ging hij aansluitend Gezondheidswetenschappen studeren aan de Radboud Universiteit Nijmegen, om deze studie na één jaar weer te staken om als waarnemend fysiotherapeut werkervaring op te doen in verpleeghuizen (Nederland), ziekenhuizen (Engeland) en een particuliere praktijk (Duitsland). In 1998 vond hij zijn eerste vaste baan in het Centrum voor Revalidatie De Vogellanden te Zwolle. Hier specialiseerde hij zich in de neurorevalidatie in het algemeen en de CVA-revalidatie in het bijzonder. In 2001 besloot hij zijn wetenschappelijke scholingsambities alsnog te verwezenlijken door aan de KU Leuven (België) de opleiding tot "Master of Physiotherapy" te gaan volgen. In 2004 behaalde hij hier zijn master's degree met groot lof (*magna cum laude*). In de jaren daaropvolgend werkte hij in zijn vrije tijd de resultaten

van de tijdens zijn masterstudie opgezette multicenter randomized controlled trial (RCT) uit tot twee internationale en één nationale publicatie(s). Van 2008 t/m 2013 was hij, naast zijn werk als fysiotherapeut in De Vogellanden, parttime als extern onderzoeker verbonden aan de afdeling Revalidatiewetenschappen van het Universitair Medisch Centrum Groningen. In deze periode hield hij zich o.a. bezig met het ontwerpen en coördineren van zijn tweede multicenter RCT, was hij betrokken bij de herziening van de Richtlijn Beroerte van het Koninklijk Nederlands Genootschap voor Fysiotherapie (KNGF) en werkte hij gestaag aan de voltooiing van zijn proefschrift. Sinds september 2011 is Lex werkzaam als docent aan de opleiding Fysiotherapie van de Hanzehogeschool Groningen.

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